THE

Journal of Obstetrics & Gynaecology of the British Empire

VOL. 55, No. 5 NEW SERIES OCTOBER 1948

ON THE CHOICE OF TREATMENT OF INDIVIDUAL CARCINOMAS OF THE CERVIX BASED ON THE ANALYSIS OF SERIAL BIOPSIES

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IT is an unfortunate but undeniable fact that out of every 100 women with carcinoma of the cervix who present themselves for treatment about 75 die of cancer within 5 years. Further, it is quite certain that by no means all the patients who die present themselves at a time when the growth is too advanced to give any hope of a cure, for anyone who has had much experience of this disease must have seen patients with tumours limited to the cervix, who about 18 months to 2 years after radium therapy have presented themselves at the follow-up clinic with a local recurrence. Such an event naturally causes the surgical enthusiast to be certain in his own mind that radical surgery would have prevented this happening, and may even lead an ardent radiotherapist to entertain doubts concerning the efficacy of radium in such a case. It is not unnatural, therefore, that in recent years there should have been a renewed interest in the use of radical surgery in the treatment of carcinoma of the cervix. The difficulty of selecting patients for radical surgery is well known and selection is mostly based on the personal impressions of the surgeon who is to perform the operation. He usually tends to select younger, fit women with tumours confined to the cervix. In such cases the results of an adequate radical operation are good, but it is by no means certain that such results could not have been achieved with radium at less risk

* Working with a grant from the British Empire Cancer Campaign.
†Working with a grant from the Northern Council of the British Empire Cancer Campaign.

to the patient. On the other hand the radiotherapist, confident that he could cure every case of this type, must be quite surprised to find ultimately, in a certain percentage of even such early tumours, a recrudescence on the cervix.

The introduction by one of us (A.G.) of the cell-count technique of determining whether or not the response of a tumour to radiotherapy was favourable appeared to offer a rational basis of selection of patients who would be unsuitable for treatment with radiotherapy alone and to attempt to salvage by surgery as many patients with radio-incurable tumours as possible. In a series of several hundreds of cervical carcinomas the prognosis regarding the local results of treatment was based on the histological assessment of serial biopsies obtained before and during irradiation, and since the clinical findings after 2 to 5 years confirmed this prognosis in about 90 per cent of cases (Glucksmann, A., and Spear, F. G., 1945, and unpublished data) the cell-count technique appears to be a reliable procedure. We have used this method continuously since December 1946, and this preliminary communication describes our clinical and pathological experiences in a group of 88 cases with an unfavourable cytological response to radium and indicates the possibility of employing surgery in dealing with this type of case. In this series we have tried to reduce the personal element by confining the work to as few persons as possible. The clinical work has been carried out by one of us (S.W.) who acknowledges the assistance of Dr. R. Dearing and Dr. W. Ross, while the histological work has been in the hands of one of us (A.G.) and thus we have, as far as possible, achieved uniformity throughout the series.

During the period under review (December 1946 to June 1948) 149 cases were studied, whilst at the same time 53 other cases were treated but were not studied. Fifty-two of these were in stages 3 and 4, and one in stage 2. This latter patient was suffering from congestive heart failure which proved fatal 1 month after admission.

All cases were submitted to cystoscopy before treatment, but shortage of diagnostic X-ray facilities made it impossible to submit every patient to routine radiographic examination of the chest, spine, and urinary tract, although all cases submitted to operation subsequent to radium were examined in this way.

Staging.

Our staging criteria are as follows:

Stage 1. The tumour is limited to the cervix.

Stage 2. The tumour invades the vaginal vault and/or extends into one or both broad ligaments, but this extension is not fixed to the pelvic wall.

Stage 3. The tumour invades the lower third of the vagina and/or extends into one or both broad ligaments and the extension is fixed to the pelvic wall.

Stage 4. The tumour invades the bladder or the rectum, or there are remote metastases.

It is impossible to determine clinically whether or not the lymph nodes are involved, and the staging therefore refers to the primary tumour and its immediate extensions only.

It is not our practice when dealing with endocervical tumours to place them in a stage lower than the clinical findings suggest, as is customary in some clinics.

In assessing cystoscopic appearances, obvious ulceration or hypertrophic tumour and massive bullous oedema are interpreted as indications of bladder involvement but the presence of generalized oedema of the bladder base is not regarded as such.

Method of obtaining biopsies. Young

areas of tumour are essential for cytological study, and therefore the area selected for section must be taken from the growing edge of the tumour. Masses of necrotic material broken off with the finger are not suitable. The cervix is drawn down with a volsellum and a small wedge cut from the tumour edge with a knife. Biopsies must not be taken with diathermy as the heat generated destroys the cellular structure. The specimen is immediately placed into a tube containing Sausa fixative, in which it is left for 3 hours before being transferred to 80 per cent alcohol. The subsequent biopsies taken during irradiation are slightly more difficult to obtain owing to shrinkage of the tumour and contraction of the vault, but usually no serious difficulty is encountered. This procedure can quite easily be carried out by any gynaecologist who is accustomed to operate on the cervix, and out of a total of 149 cases, only in 7 instances has a prognosis not been possible because of a totally inadequate biopsy. It is, however, not a procedure which should be left to a junior house surgeon.

Radium technique. The method of irradiation used at first was a modification of the Stockholm technique in which a dose of not less than 7,500r was delivered to "point A" in two equal doses separated by an interval of 7 days. The dose received on the surface of the tumour is not less than 10,000r and often more than 13,000r. This technique was adopted during the war when bed accommodation was severely limited, but since November 1947 we have reverted to a 3-dose technique with a week's interval between the first and second, and a 2 weeks' interval between the second and third applications. The total dose remained the same but was given in an over-all time of 23 instead of 10 days.

Surgery. The extent of the radical operation is based on the technique described by Comyns Berkeley and Victor Bonney (1935) and consists of the removal of the uterus, Fallopian tubes, and ovaries and the upper nine-tenths of the vagina, the broad ligaments, the pelvic connective tissue and the lymph nodes lying along the course of the external and internal iliac vessels and the obturator node. If these nodes are obviously involved the dissection is carried up to the aortic bifurcation and higher if necessary. Continuous blood transfusion is given throughout the operation and spinal anaesthesia is supplemented by sufficient inhalation or intravenous anaesthesia to keep the patient asleep.

Our present procedure is as follows:

The patient is examined under anaesthesia and the tumour staged, the preliminary biopsy taken and the first application of radium given. A week later a second biopsy is taken and the second application of radium given. During the following 2 weeks' interval the histological analysis is made and the prognosis obtained. In the few cases where a further biopsy has appeared advisable this was taken during this interval.

If the prognosis is favourable the third application of radium is given, followed 2 weeks later by bilateral iliac adenectomy and in a series of 10 cases thus treated so far only 1 showed node involvement.

If the prognosis is unfavourable and the case is suitable for radical surgery then no further radium is given and a radical hysterectomy is performed 6 weeks later. If, however, the prognosis is unfavourable and the tumour is inoperable a further application of radium is given but iliac adenectomy is not performed.

At first a full dose of radium was given before operation, but it was found that the combined treatment was sometimes followed by massive pelvic necrosis. After this experience in the next 7 cases, the first dose only was given and operation performed 2 weeks later. This proved even more un-

satisfactory as it entailed removing a necrotic infected cervix and was followed by very severe pelvic sepsis leading to the death of 3 patients. As a result of this experience the technique described above was adopted, since when there has been only 1 case of necrosis and no postoperative deaths.

Quantitative histological analysis of serial biopsies. The following principles are adopted for the interpretation of histological appearances: young areas are selected for analysis in each biopsy and the cell population of these selected foci is counted in 4 categories: resting (potential dividing "stock" cells), mitotic, differentiating (mainly keratinizing and parakeratotic cells), and degenerating cells. The detailed histological methods employed and the general characters of the 4 cell types have been described previously (Glucksmann, A., 1947).

In cases in which the tumour fails to respond to irradiation treatment the histological picture before and after exposure to radium is approximately the same. There is usually actively growing tumour tissue present after a dose of about 4,000r to 5,000r and these histological appearances would be reported as active growth by any pathologist. Though the growth of such tumours may be slowed down temporarily by inhibition of division of tumour cells, by vascular damage or by the often developing fibrosis, this retardation of growth very rarely suffices to bring about a "cure", but may delay the recurrence of symptoms.

In order to recognize the histological features of a favourably responding tumour a good deal of experience and a detailed acquaintance with normal and pathological cytology is necessary. While general principles can be laid down for the assessment of viability of cells, their application to the individual tumour necessitates the introduction of various modifications.

A favourable response of the tumour tissue to irradiation is indicated by the complete elimination of viable cells (resting and mitotic) and their replacement by nonviable (differentiating and degenerating) cells. In such cases there is an increase not only in the percentage of differentiating cells but also in the degree of differentiation (i.e. a nearer approach to the normal stages in keratinization), and usually a marked increase in the incidence of abnormal mitotic and of degenerating cells. It has been found, however, that in epitheliomatous growths a mere marked increase in necrosis, without an increase in differentiation, rarely suffices to effect a "cure". In favourable cases no normal mitotic cells should be found 7 days after the first radium insertion and the percentage of resting cells should have fallen to below 30; while the percentage, particularly of differentiating, but also of degenerating cells, should have risen correspondingly.

Minor variations in the percentage of viable cells such as their reduction by 20–30 per cent 7 days after a dose of about 4,500 to 5,000r at the biopsy site are considered as partial responses and interpreted as an ultimately unfavourable prognostic sign.

Since in the treatment of cervical cancer the dose distribution in the pelvis is uneven, a favourable prognosis given for the fully treated primary tumour may not apply for an involved lymph node which on account of its distance from the radium source has been insufficiently treated. A favourable prognosis holds, therefore, only for the fully treated region. An unfavourable prognosis for the tumour at the biopsy site applies, of course, also to the less fully treated regional nodes.

The clinical results of treatment can be assessed with some certainty only after a considerable interval and for this reason the "five years symptom-free survival rate" is generally adopted. This delayed assess-

ment of clinical results implies that recurrence of symptoms due to persistence of tumour tissue may be postponed for periods of years and it is generally true that this delay is the shorter the more advanced the tumour was at the beginning of the treatment. It is thus not surprising to find no clinical signs of disease during the first years after treatment in stage 1 and 2 cases even though there is histological evidence of persisting tumour activity. In those cases of the present series where, following an unfavourable histological prognosis a Wertheim's operation was performed 8 weeks after a full course of radium therapy (Table IV, cases 1–15) active tumour tissue was found in the cervix of all operation specimens. In the other surgically treated cases which received only one-third or two-thirds of the full radium dosage, active tumour tissue was found in the cervix in all but one case. In this exceptional case only part of the cervix was available for histological examination, but a number of associated lymph nodes were involved.

The best example of persisting tumour activity giving no clinical symptoms was found in the first case in the series, where two months after completion of a full course of radium therapy the cervix appeared clinically healed. When it was cut open after hysterectomy a mass of active tumour 1 cm. in diameter was found underneath the intact mucosa. The estimated dose of radium received by this particular area was 18,000r. This patient is still alive and well 20 months after operation, but it is doubtful if she would have been if we had waited for clinical evidence of recurrence (See Plate).

It has been found previously (Glucksmann, A., and Spear, F. G., 1945) that the differentiated types of cervical tumours tend to respond favourably in a greater proportion of cases than do the anaplastic types. In the present series the tumours were therefore also classified on the basis of the pre-treatment biopsy as to their degree of anaplasia judged by the histogenesis of the tumour tissue, by its morphological and cytological differentiation and by the amount and type of stroma induced. On the basis of this classification the tumour was assigned to the anaplastic (A) or differentiating (D) group.

The 5-year symptom-free survival rate of differentiated cervical tumours is greater than that of anaplastic tumours of equal clinical extent. It is, however, the capacity to respond to irradiation with an increase in extent and degree of differentiation, rather than the amount of differentiation already present in the untreated tumour, which often distinguishes the radio-curable from the radio-incurable tumours. This capacity for increased differentiation as a result of irradiation may be latent in an untreated anaplastic tumour; on the other hand it may have reached its full limit in the untreated differentiated tumour. This capacity, therefore, can be judged only by the behaviour of the tumour tissue before and after an exposure to a "test dose" of radiation.

In the present series of cases, 32 tumours gave a favourable response and of these

25 were of the differentiating type (per cent 78 ± 7.3) while

7 were of the anaplastic type (per cent 22 ± 7.3).

Of the 88 cases giving an unfavourable response, 4 were adenocarcinomas, and of the remaining 84 epitheliomas

20 were of the differentiating type (per cent 24 ± 4.7) while

64 were of the anaplastic type (per cent 76 ± 4.7).

The difference in the incidence of differentiating and anaplastic tumour types between cases giving a favourable and those giving an unfavourable response is per cent 54 ± 8.7. Conversely, of 45 differentiated

tumours 25 (per cent 56 ± 7.4) gave a favourable response, while only 7 of 70 anaplastic tumours (per cent 10 ± 3.6) responded favourably. The difference in favourable response to treatment between differentiating and anaplastic tumour types of this small series amounts to per cent 46 ± 8.2.

Operability-rate. Of 149 cases studied 32 showed a favourable histological response to treatment, in 22 the response was probably favourable, and in 7 it was not possible to obtain a prognosis on account of inadequate biopsy material. In 88 the prognosis was definitely unfavourable and it is with these patients that we are concerned in the remainder of this paper.

TABLE I.
Stage Distribution and Operability of Radio-incurable Cases.

STAGE 1			
	Operable	9	
	Technically operable	3	
	Inoperable	0	12
STAGE 2			
	Operable	32	
	Technically operable	15	
	Inoperable	3	50
STAGE 3			
	Operable	4	
	Technically operable ...	0	
	Inoperable	13	17
STAGE 4			
	Inoperable	6	6
STUMP			
	Operable	1	
	Inoperable	2	3
	Total		88
	Total operable	46	
	,, technically operable	18	
	,, inoperable	24	

Table I shows the distribution in stages of the 88 patients whose response to radium was assessed as unfavourable, and shows also the operability as judged by examination under anaesthesia and cystoscopy. By " technically operable " we mean that operation was contra-indicated on account of concomitant disease or advanced age, but as far as the local condition was concerned it appeared possible to remove the tumour. Our estimated operability rate was then 52 per cent.

It must be remembered that during the same period 53 cases were not studied by serial biopsies, as they were considered inoperable; but against this, account must be taken of 54 other cases in which the response to radium was favourable or probably favourable, because these latter cases were operable and therefore our maximum estimated operability remains at 52 per cent. All except 1 of the 53 inoperable cases which were not submitted to a cytological study were in stages 3 and 4 and we have no case in this category so far which has shown a favourable response to radium, and therefore we may assume that all these cases would have responded unfavourably. Since it was this very type of case upon which we wished to operate it is therefore probable that our true operability rate would have been 46 cases out of 141 (88 + 53) or 33 per cent; and when we further take into consideration the fact that 10 of our supposed operable cases were found to be inoperable at laparotomy our operability-rate in these unfavourable cases was reduced still further to 26 per cent.

As Table II shows, of the 88 cases which responded unfavourably to radium we succeeded in completing the radical operation in only 28 cases, or 32 per cent. Three other cases were not operated on because they had been given a full therapeutic dose of radium, and by the time they came to operation we had found a high incidence of necrosis when operating on cases which had been fully irridiated. Three others were made inoperable by inflammation and necrosis following radium therapy. In 2 others the tumour did not regress in spite of full radium treatment but had become so extensive that any possibility of opera-

TABLE II.
Surgical Treatment of "Operable" Cases.

Wertheim's hysterectomy completed		28
Wertheim's hysterectomy abandoned on account of:		
Fixed nodes	5	
Fixation of cervix to bladder	3	
Fixation of cervix and fixed nodes	1	
Inflammation and necrosis ...	1	
		10
Wertheim's hysterectomy not considered on account of:		
Radium necrosis	2*	
Change in radium technique	3*	
Death from intercurrent disease before operation	1	
Too rapid extension of tumour between radium and operation	2*	
		8
Total		46

* Cases included in results in Table III.

tion had disappeared 8 weeks after radium treatment. These 2 patients had very anaplastic tumours which are often thought to be particularly radiosensitive.

The incidence of node involvement. The effect of the presence of growth in the regional lymph nodes on the prognosis is well known. Bonney (1941) has shown that whereas he was able to obtain a 53 per cent 5-year cure rate in cases where the regional nodes were not involved, this figure was reduced to 22 per cent in cases where the nodes were involved. It is obvious, therefore, that the chances of survival are greatly reduced when the tumour has metastasised to the regional nodes.

In this series of Wertheim operations there were 16 cases in which the nodes were involved and 12 in which they were not involved. In addition, in 9 out of 10 inoperable cases on which laparotomy was performed the nodes were microscopically involved, and in the tenth they were not removed, and it is not known whether they contained tumour. Therefore, in 37 cases in which we have microscopic sections the nodes were involved in 25, or 68 per cent. This is a much higher incidence of node involvement than the 40 per cent quoted by Bonney for his entire series (difference per cent, 28 ± 8.0).

It would appear that the type of tumour which responds badly to treatment by radiation frequently metastasises to the regional nodes and this coupled with the comparatively low operability-rate must reflect inevitably on the ultimate result. Since these patients are doomed in any case such survivors as there may be will owe their lives to surgery.

The fate of the cases not treated surgically. Table III shows the fate of the unfavourable cases upon whom operation was not performed. Briefly, if those who are dead with cancer, or living with a recurrence, are classified as unsatisfactory, and those who are living without clinical evidence of recurrence are called satisfactory, then to date (that is 3–20 months) after treatment, 24 (49 per cent) can be described as satisfactory, and if the 10 cases

TABLE III.
Fate of Cases not Treated Surgically.

	Alive	Dead	Alive with rec.	Died intercurrent	Total
	Treated more than six months.				
Stage 1	3	0	0	0	3
Stage 2	14	4	2	1*	21
Stage 3	2	3	4	0	9
Stage 4	0	2	2	0	4
Stump	1	0	1	0	2
	20	9	9	1	39
	Treated less than six months				
Stage 1	1	0	0	1	2
Stage 2	1	0	1	0	2
Stage 3	2	0	2	0	4
Stage 4	0	0	2	0	2
	4	0	5	1	10

* Active growth on cervix at autopsy.

TABLE IV.

Fate of Surgically Treated Cases.

No.	Age	Clinical stage †	Tumour type (1)	Radium dose (2)	Interval (3)	Tumour in (4) cervix	Tumour in (4) nodes	Result
1	39	2	D	Full	8	+	+	Secondary operation for groin nodes. Alive and well 20/12.
2	41	2	D	Full	8	+	+	Alive and well 20/12.
3*	28	3	A	Full	8	+	+	Died 1 year; recurrence at vulvo-vaginal junction with groin nodes
4	57	1E	D	Full	8	+	+	Died 10 days; massive collapse of lung. Autopsy: no growth.
5	60	2	D	Full	8	+	–	Alive and well 15/12.
6	36	2	A	Full	8	+	–	Alive and well 14/12.
7*	41	2	A	Full	8	+	–	Alive and well 12/12.
8*	50	2	A	Full	8	+	+	Died 12/12; lung metastases.
9*	51	1	A	Full	8	+	–	Died 5/12 following ureteric transplant for fistula. Autopsy: no growth.
10	39	2	A	Full	8	+	–	Alive and well 12/12.
11	33	1	A	Full	8	+	+	Died. Abdominal recurrence 8/12.
12	56	2	A	Full	8	+	+	Alive, no recurrence 10/12. Has metastases from concurrent breast primary.
13	53	1E	A	Full	8	+	–	Died 9/12. Metastases mediastinum.
14	49	2E	A	Full	8	+	–	Alive and well 10/12.
15	47	2	A	Full	8	+	+	Alive and well 9/12.
16	61	2E	A	$\frac{1}{3}$	2	+	–	Died 1 month; pyelonephritis. Autopsy: no growth.
17	40	1	D	$\frac{1}{3}$	2	+	–	Alive and well 9/12.
18*	49	2	A	$\frac{1}{3}$	2	+	+	Alive 9/12; fistula.
19	53	2	D	$\frac{1}{3}$	2	+	+	Alive and well 6/12.
20	55	2	A	$\frac{1}{3}$	2	+	+	Alive and well 6/12.
21	46	2	A	$\frac{1}{3}$	2	+	–	Died 14 days; pyelonephritis and pulmonary embolism. Autopsy: no growth.
22	57	2E	A	$\frac{1}{3}$	2	+	+	Died 10 days pneumonia. Autopsy: no growth.
23	60	1	D	$\frac{2}{3}$	6	–	+	Alive and well 3/12.
24	54	2E	A	$\frac{2}{3}$	6	+	–	Alive and well 3/12.
25	49	2	A	$\frac{2}{3}$	6	+	–	Alive and well 3/12.
26	43	2	A	$\frac{2}{3}$	6	+	+	Alive and well 3/12.
27*	36	3	A	$\frac{2}{3}$	6	+	+	Alive 3/12; fistula.
28	33	2	A	$\frac{2}{3}$	6	+	+	Alive and well 3/12.

(1) D—Differentiating tumour. A—Anaplastic tumour.
(2) Full = full course of 2 stage modified Stockholm technique.
$\frac{1}{3}$ = one dose of 3 stage modified Stockholm technique.
$\frac{2}{3}$ = two doses of 3 stage modified Stockholm technique.
(3) Interval (in weeks) between radiological and surgical treatment.
(4) Presence of active tumour tissue in operation specimen.

* These cases developed necrosis subsequent to operation.

† The letter E placed after the stage No. indicates that the tumour is endocervical.

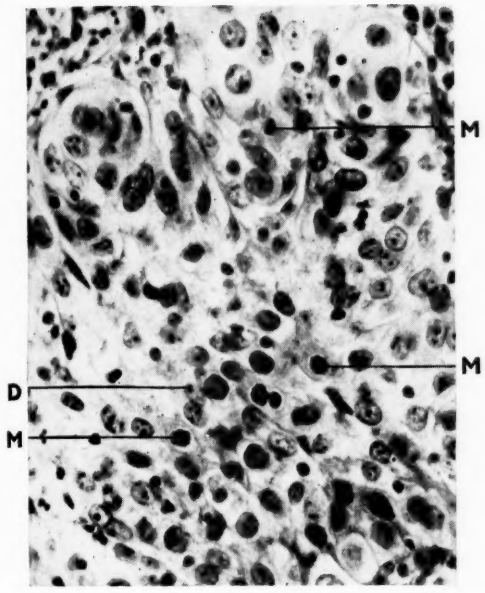

FIG. 1.

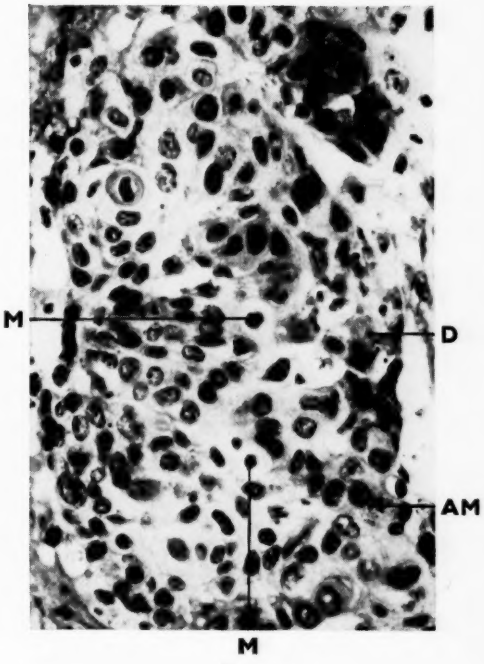

FIG. 2.

DESCRIPTION OF FIGURES.

The microphotographs 1–4 illustrate the histological features observed in the biopsies and in the operation specimen taken from a patient with carcinoma of the uterine cervix, clinical stage 2 (cf. Table IV, case No. 1). Fig. 1 shows the tumour before radiation treatment; Fig. 2 reproduces a comparable tumour focus 7 days after the first radium insertion, i.e., after an estimated dose of 9000r at the biopsy site. Fig. 3 illustrates the tumour mass found under the intact mucosa 8 weeks after a full course of radium treatment, i.e., after an estimated dose of 18,000r at this site. Fig. 4 shows a comparable young tumour focus in the right external iliac lymph node.

Figs. 1–4 are reproduced at a magnification of × 350.

It will be noted that apart from slight variations in cell size and from slight increases in the incidence of abnormal mitotic and of degenerating cells (cf. in particular Fig. 2), the activity of the tumour tissue of this patient is not checked by exposure to radium.

List of abbreviations:

AM = Abnormal mitotic cell. D = Degenerating cell.
M = Normal mitotic cell.

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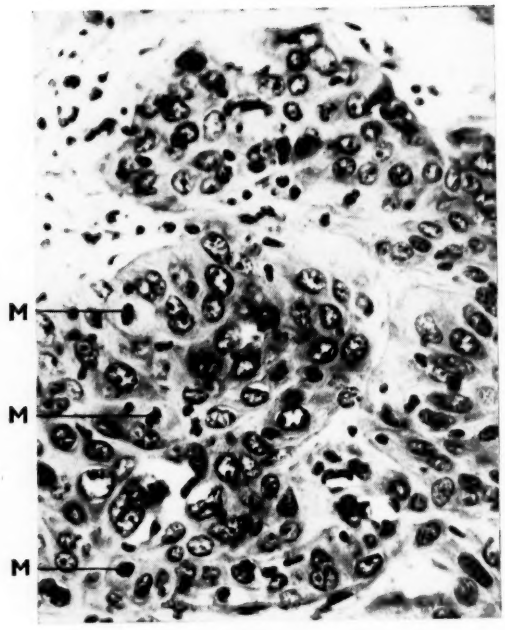

FIG. 3.

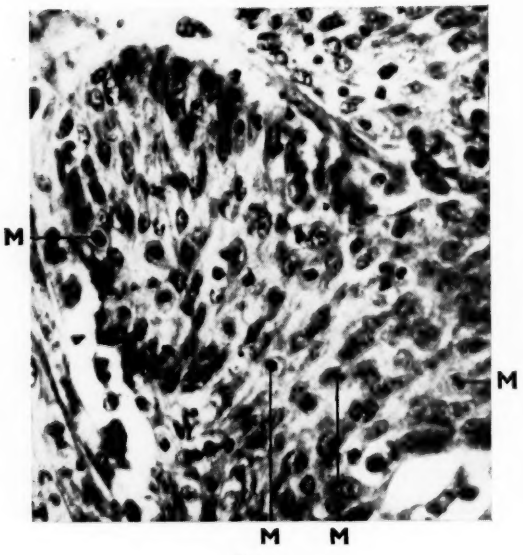

FIG. 4.

upon whom operation was attempted but could not be carried out are included then the percentage of satisfactory results to date is only 41.

The fate of the surgically treated cases. Table IV shows the results of these cases. If we use the same criteria as when dealing with the group just described we have, to date, 18 satisfactory cases, and 1 who is satisfactory as far as the cervical tumour is concerned but who has metastases from another treated primary tumour (breast), then we have 19 satisfactory cases (68 per cent) and 9 unsatisfactory.

The influence of node involvement is already apparent, for of 13 node-involved cases surviving operation, 3 are already dead, whereas of 10 cases without node involvement only 1 has, so far, died of cancer. It should be observed that operative deaths, and the remote operative death where we obtained autopsy evidence of the absence of tumour, are included in the unsatisfactory group of cases.

Discussion.

We believe that provided (1) the tumour is of the type that responds to radiotherapy, and (2) that it is of such an extent that every part of it can be adequately irradiated, then radium can achieve more in the cure of the primary tumour than the Wertheim's operation and with less risk. If the first of these conditions is not fulfilled then surgery is the only hope of saving the patient. If the second cannot be fulfilled then possibly a combination of radium and surgery is the answer, but that is a problem beyond the scope of this paper.

Unfortunately it appears that a rather large percentage of unfavourably responding tumours are found in patients who are not best suited for a surgical attack. Of our stage 1 tumours, 69 per cent responded favourably, and all the cases in which we found a favourable response were operable. In addition to this we have found a high incidence of node involvement in the unfavourably responding tumours, the adverse influence of which is too well known to need repetition. It would seem that the cases known to do well with Wertheim's operation, namely early tumours without node involvement and often of a well-differentiated type, are also the cases that do well with radium. Nevertheless it does appear that surgery still has an important part to play in the treatment of carcinoma of the cervix. Bonney and others have shown that some cases with node involvement can be cured and some of our surgically treated cases at least have a chance of survival, whereas their prospects without operation were hopeless, since all had active tumour tissue present at operation. We believe, however, that it is unjustifiable to submit a patient to surgery without first determining the response of the tumour to radiation.

The time seems ripe for a new approach to this very important problem. For too long too many people have regarded surgery and radium as the methods of opposing camps. Nothing could be further from the truth. Some tumours are suitable for treatment with radium and some are not. For these latter patients surgery, at the moment, is the only alternative treatment, but there remains, unfortunately, a group of cases who are beyond the hope of either method and to find a way of dealing successfully with such patients is an urgent challenge to further combined scientific and clinical research. If, however, the other patients are to derive the maximum benefit from existing methods of treatment it is essential that the most suitable technique be selected for each individual tumour, and we believe that our approach offers a rational basis for such individualization.

SUMMARY.

1. The response of individual cervical carcinomas to radiotherapy was determined by a quantitative histological analysis of serial biopsies.

2. An attempt was made to salvage, by surgery, patients with tumours not responding to a test dose of radiation.

3. Of 149 cases studied 54 gave a favourable or probably favourable response; 88 gave an unfavourable response, and in 7 the biopsy material provided was inadequate. In the 54 favourably responding cases, radium alone was used in the treatment of the primary tumour, but in a small number the regional lymph nodes were removed surgically. Of the 88 unfavourable cases 46 were initially considered suitable for Wertheim's hysterectomy, which was completed in 28 cases (Table II).

4. In 37 cases with unfavourably responding tumours in which the pelvic lymph nodes were examined microscopically, tumour tissue was present in 25. In 22 of these patients the primary tumours were in clinical stages 1 and 2 and the remainder in stage 3.

5. Though in patients with *radio-incurable* tumours of the cervix, the high incidence of lymph node involvement and the comparatively low operability-rate must limit the success of radical surgery, it is at present the only effective means of dealing with this type of tumour.

REFERENCES.

Berkeley, C., and Bonney, V. (1935): *A Textbook of Gynaecological Surgery*, 3rd edition, page 336, Cassell, London.

Bonney, V. (1941): *J. Obst. Gynaec.*, **48**, 421.

Glucksmann, A., and Spear, F. G. (1945): *Brit. J. Radiol.*, **18**, 313.

Glucksmann, A. (1947): *Recent Advances in Clinical Pathology*, page 338. Churchill, London.

THE VASCULAR PATTERN OF THE PLACENTA AND ITS DEVELOPMENT IN THE RAT

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IN his detailed investigation of the development of the rabbit's placenta, Mossman (1926) studied in particular the arrangement of both foetal and maternal blood-vessels in relation to each other, and pointed out the significance of the vascular dispositions. He had been preceded in this study by the work of Tafani (1887) who recorded the same arrangement of vessels in the placentae of the cat, dog, guinea-pig, and rabbit. Tafani, however, presented his observations without significant comment or illustration. Recently, Barcroft and Barron (1946) studied the cotyledonary placenta of the sheep, and showed that, as in the rabbit, the blood-flow in the maternal capillary bed is parallel with, but opposite in direction to, that in the foetal capillaries; they correlated their anatomical observations with the changes which occur during gestation in the oxygen-saturation of the blood passing along the umbilical vein. At the same time, direct experimental evidence was produced by Noer (1946) in support of Mossman's hypothesis on the physiological effects of this anatomical arrangement, so that this theory may be considered as definitely established. In his survey of placentation Mossman (1937) indicated that the arrangement of the foetal and maternal vessels was determined by the mode of invasion of the allantoic villi. Unlike the rabbit, implantation in the rat is antimesometrial, although the allantoic placenta is formed on the mesometrial side of the uterus, and so it was thought that it would be of interest to see if the maternal circulation conforms to the same pattern, and, if so, how such an arrangement is established.

Many studies have already been made of the placenta and placentation in the rat and the mouse, notably that of Duval (1891). Its histology has also been well covered by Jenkinson (1902) on the glycogenic cells, both maternal and foetal, and Krehbiel (1937) on the decidual cells, in the so-called "deciduomata". Grosser (1909, 1927) and Mossman (1937) provide good surveys and bibliographies on the placenta generally. Consequently, relatively little attention is paid to many of these details in this communication.

Observations have also been made on the maternal blood-vessels in the earliest stages of placentation in the sheep as well as a few on those of the placentae of the cat and pig.

MATERIAL AND METHODS.

The routine injection mass consisted of dried human plasma unfit for human use.

This was reconstituted as directed on the bottles to normal concentration, using 10 to 20 per cent Indian ink instead of distilled water. The mixture was quickly filtered through cotton wool, and would keep for a considerable length of time provided that it was filtered immediately before use. It flowed easily and had the advantage over gelatin masses that it could be injected cold. On fixation the plasma proteins became coagulated in the vessels and retained the ink within them. The only drawback was that in the larger vessels, especially the veins, the mass tended to fall out on sectioning, leaving, however, a distinct black annulus around the walls of the vessels (Fig. 14). This did not occur with the smaller vessels, and so did not materially reduce the value of the technique. The rats and cats were injected through the descending aorta, the former immediately after being killed by coal gas, the latter within an hour or two of death by chloroform. The extirpated uteri of the sheep and pigs were obtained from slaughter-houses and were injected through the uterine arteries. The hydrostatic pressure used was about 100 mm. mercury. It was not found necessary to wash out the blood from the vessels before injection. When injection was considered adequate, the specimen was immersed in either 10 per cent unneutralized formalin or Bouin's fixative for 24 hours; the uteri were then removed from the cats and rats and replaced in the fixative for 24 hours, or until required. Blocks of the uteri or placentae were embedded in celloidin, sectioned at thicknesses of 40 to 100μ and stained lightly with haematoxylin, neutral red, saffranin or Biebrich scarlet. With the pig uteri, as well as sections cut in celloidin, several free-hand sections of about 200–200μ were cut, dehydrated, cleared in oil of wintergreen and examined under the binocular microscope. Some sections were also cut at 5 and 10μ in paraffin, and stained with Delafield's haematoxylin and eosin or iron haematoxylin. A complete series of histological preparations of rat placentae, stained with haematoxylin and eosin, was also used.

In the case of the rat, the ages of the embryos were accurately known. Daily vaginal smears were taken, as described by Long and Evans (1922), and a male was placed in the cage overnight when the female was coming on heat. Next morning, the female was examined for signs of a vaginal plug or sperms in the smear. The females were then killed at the desired stage. With all the other animals no histories were available and size of embryo was the only guide to age.

With some of the rat uteri in the earlier stages of gestation, the injection of Indian ink was followed by the injection of a sus-

TABLE I.

	Age of embryos in days	Injected specimens	Uninjected specimens
RATS	Non-pregnant	R18	W245
	7	R17	—
	8	R16	R22
			W286
	9	R9	W285
	10	R11	W283
	11	—	W277
	12	R15	W243
	13	—	W251
			W289
	14	R4	W294
	15	—	W234
	16	—	W250
	17	R8	W227
			W275
	18	R10	W299
	19	R14	W296
	20	R12	W274
			W304
SHEEP		10 mm.	17 mm.
		10 mm.	20 mm.
		27 mm.	
		28 mm.	
		31.5 mm.	

pension of starch granules which filled the arteries. The starch was subsequently stained in the sections with iodine, and thus provided a differential injection of the arteries and veins. In later stages, however, this technique was not used as considerable quantities of starch passed into the venous circulation. Details of the material used are listed in Table I.

In addition there were 2 injected and 1 uninjected barren uteri, and an injected uterus which contained a blastocyst of moderate dimensions, which were unfortunately not recorded.

Cat.

The material consisted of 5 injected uteri, 2 non-pregnant and 3 each containing 5 foetuses, the average crown–rump lengths being 93, 108 and 116 mm., i.e., near term.

Pig.

The material consisted of several barren uteri and 1 pregnant uterus containing 11 foetuses of crown–rump length 70 mm. (one a cyclops), as well as 2 macerated and partially resorbed foetuses.

The Rat.

Gross arrangement of uterine blood-vessels. The uterine artery runs in the mesometrium parallel with, and about 5–10 mm. distant from, the uterine horn, and anastomoses cranially with the ovarian artery supplying the Fallopian tube. The uterus receives its blood-supply by a series of arteries—about 12 in number—which spring from the uterine artery, at right angles to it, in a regular series, and pass towards the uterus. Shortly before reaching it each of these vessels divides into two or three branches which join those from the neighbouring arteries to form an anastomosing arcade alongside the uterus, from which a host of small arteries spring at all levels to supply this organ. The blood-supply is rich and the veins which accompany the arteries very prominent. The pattern is quite characteristic and is easily distinguished from that of the intestine.

The non-pregnant uterus. The outer longitudinal and inner circular muscle coats are clearly defined. Whereas the latter completely encircles the uterus, the former extends out into the mesometrium for about 2 mm. and then comes to an abrupt end (Fig. 1). The tissue between these 2 layers of longitudinal muscle consists of a stroma similar to that within the endometrium, but interspersed with muscle fibres. Within it are the numerous small arteries or arterioles which supply the uterus, as well as the much larger and less frequent uterine veins, which join with those from the opposite side of the uterus between the two muscle layers. At the limit of the muscle, this tissue becomes transformed abruptly into the fat-laden cells of the mesometrium. During pregnancy, the uterus swells considerably, and these two layers of longitudinal muscle are gradually taken up into the uterine walls, whilst the intervening tissue hypertrophies and takes part in the formation of the "noyau mediomusculaire" (Duval) or the "myometrial gland" of most other authors, which appears as a prominent bulge on the mesometrial side of the uterus in the latter third of pregnancy.

The arteries, entering the uterus between these two layers of longitudinal muscle, continue in a tightly spiralled manner around its wall, between the muscle coats, anastomosing antimesometrially (Fig. 1). They send branches outwards through the longitudinal muscle, supplying it and forming loops under the serous coat. More numerous branches also pass radially through the circular muscle, and enter the

outer, or basal, part of the endometrium. So far, these branches are coiled, but, as they pass inwards, they become straight, and almost reach the uterine epithelium before they break up into a terminal capillary plexus underneath it (Figs. 1 and 2). At the mesometrial side of the uterus, these inwardly-directed arteries are more numerous and pass into the stroma through the circular muscle, which is somewhat thicker at this point, directly from the "muscular" mesometrium.

These latter arteries present an interesting appearance in the injected specimen, R18. The injection mass is apparent right up to the circular muscle, and then it almost disappears where the arteries lie within the muscle, promptly reappearing when they reach the uterine stroma. Although this phenomenon may be due to an agonal postmortem contraction of the muscle (or contraction induced by fixation) it suggests the possibility of a sphincteric action on these vessels by the circular muscle, and will be considered later.

The veins within the uterus are very voluminous; the main ones lie in the outer or basal part of the endometrium, close to the circular muscle. Much smaller veins, draining the longitudinal muscle and serosa, accompany the arteries between the muscle coats. The large veins pierce the circular muscle obliquely, shortly before reaching the mesometrial attachment to the uterus (Fig. 1).

In the resting state the uterine epithelium is cubical or low columnar and thrown into large folds. The thickness of the subepithelial tissue of the endometrium is about 800μ at the crests of the folds, and 400μ at the troughs. It is somewhat thinner on the mesometrial side, since the lumen of the uterus is eccentrically disposed in that direction. The uterine glands, neither as numerous nor as complicated as in most mammals, lie in the stroma on the lateral and antimesometrial parts of the uterus, and are absent in the mesometrial quadrant. There is thus a strip of tissue running down the mesometrial border of the uterus, where the definitive allanto-placenta will form, devoid of glands, but containing a compact leash of straight arteries running right through it from the underlying muscle to the epithelium (Fig. 2). In these two characteristics it is reminiscent of, though not so clearly demarcated as, the extremely specialized implantation areas in the bovine uterus. During oestrus, the uterus is distended by fluid, and the endometrium becomes stretched. The stroma is then about 200μ in thickness laterally, chiefly due to the presence of the glands, but only 100μ mesometrially and antimesometrially. The uterine epithelium becomes very tall at oestrus.

Seventh day of pregnancy. By this stage, the embryo has reached its final position in the uterus and has implanted; the decidual reactions around it are well established. The stroma of the uterus, or decidua as it may now be called, increases enormously around the embryo, on the lateral and antimesometrial sides of the uterus. As a result, the uterine lumen is greatly reduced in calibre, and appears to be displaced towards the mesometrial side. The embryo then lies at the antimesometrial end of a long narrow pit which runs horizontally across the uterus from the antimesometrial to the mesometrial side, its mouth opening mesometrially into the narrowed uterine lumen. In a longitudinal section of the pregnant uterus, cut parallel to a line joining its mesometrial and antimesometrial sides, the narrow uterine cavity and implantation pit, within the decidua, resemble a capital T laid on its side. The crosspiece of the T represents the slit-like lumen which unites the unrestricted regions of the uterine cavity between the implantation sites; throughout

most of its extent it is exceedingly narrow (and is soon obliterated in later stages) but in the middle it is more expansive and, from here, the vertical limb of the T, representing the implantation pit, extends away towards the antimesometrial side; in its extremity lies the embryo (Fig. 3): compare with Duval (1891, Figs. 85–87) and Grosser (1927, Fig. 127). In his Fig. 86 Duval illustrates a fold ("plis") or papilla, labelled P, projecting into the uterine lumen, opposite the mouth of the implantation pit, which he claims (page 40) takes a part in the obliteration of the uterine lumen: "Ces plis . . . contribuent à produire . . . la sondure de ces deux régions opposées de la muqueuse, de manière à oblitérer le canal utérin au niveau de chaque loge contenant un oeuf." In our sections of the present and two succeeding stages, however, this papilla shows distinct signs of degeneration. The epithelium covering it is not as tall as elsewhere and stains more deeply. The nuclei are large and dark, and occupy most of the cell body, extending from the base to the free edge. The cells of the stroma within the papilla degenerate, during the 8th day, into a homogenous eosinophilic mass containing a number of pyknotic nuclei; this retracts from the surrounding tissues (Fig. 6).

The vascular pattern of the decidua has now changed considerably. Owing to the decidual reaction, the diameter of the uterus in the mesometric-antimesometric direction has increased considerably. As a result, the main orientation of the prominent vessels is parallel to this elongation and to the walls of the implantation pit. The arteries piercing the circular muscle at all points, and formerly passing through the stroma to the subepithelial plexus, are now difficult to find. Even on the mesometrial side, elongated parallel to the implantation pit, the subepithelial plexus is dilated, increased in depth, becoming sinusoidal, prominent and engorged; in places this plexus has ruptured and released the injection mass into the lumen. This is partly due to the rather higher pressure used to produce a satisfactory injection of these earlier stages. However, as there would seem to be a normal leakage of blood through the epithelium lining the pit into the lumen about this stage, the ink in the lumen does, to some extent, represent a normal phenomenon. The embryo itself is surrounded by a zone of tissue which is virtually avascular; this corresponds to the primary decidual zone of Krehbiel (1937, Fig. 1D) who has described in detail the cytological changes taking place during the early stages of pregnancy. The large veins, lying just within the circular muscle and in the basal part of the uterine stroma, which is as yet relatively unchanged, are also dilated and prominent and show an occasional rupture. The vascular changes at this stage consist of capillary and venous dilatation and increase, together with relative insignificance of the arteries within the circle of tissue enclosed by the circular muscle. The pattern of the circulation is largely dependent on a distension of the uterus in the mesometrial-antimesometrial direction. Between the implantation sites, there is a general increase in vascularity, both arterial and venous but affecting particularly the smaller vessels and capillaries.

Eighth day of pregnancy. The general dispositions at this stage, as seen on transverse section, are shown in Diagram I. It is of interest to note that in the particular implantation from R22 which was used as the basis of the diagram, the embryo has implanted the wrong way round. The ectoplacental cone or Träger is well developed, as is the inverted yolk-sac; the first signs of the proamniotic cavity are also present. In fact, the embryo appears quite

normal for this stage of development (see Huber, 1915, Figs. 26 and 27). Nevertheless, the whole embryo is so orientated that the Träger is facing away from the mesometrium instead of towards it, whereas the germinal mass, "suspended" in the yolk-sac, is directed mesometrially. It is difficult to visualize how this embryo could have developed a successfully functioning placenta on the antimesometrial side of the uterus, for the decidual reaction does not appear to differ in any respect from the other implantation sites in the same uterus, in which the embryo has orientated itself in the usual direction. This observation is in conformity with the work done on the "deciduomata" which can be produced by artificial stimuli in the uteri of rats and other animals. It has been shown that the stimulus provided by the embryo for the initiation of the decidual reaction is not a specific one, but can be reproduced by a variety of means. Consequently, the malorientation of this particular embryo would not be expected to have, and, in fact, does not have, any effect on the development of the decidua. Because of the apparent improbability of a placenta being formed in this case, the embryo would have died about the 11th or 12th day. Hence, incorrect orientation of the blastocyst, with reference to the implantation site, would seem to be a contributory factor to intra-uterine mortality, but to what extent it is impossible to say. Malpresentation of the embryo at term is a well-recognized cause of foetal mortality but malposition of the blastocyst at implantation does not appear to have been recognized previously.

At this particular stage the whole of the decidual tissue presents three fairly obvious zones (Diagram I). The first occupies the antimesometrial half of the uterus, and almost encircles the embryo; the second occupies the mesometrial half, and surrounds the constricted uterine lumen, and the third is a narrow, transverse band between the other two zones, bordering on the side of the implantation pit (Grosser, 1927, Fig. 130). The first zone is the "decidua capsularis" and the remaining two comprise the "decidua basalis."

The capsularis, called the "caduque réfléchie" by Duval, and roughly equivalent to the secondary decidual zone of Krehbiel (1927) at this stage, is composed of a very compact mass of cells, superficially resembling liver tissue. The cells are moderately large, and tend to be oval rather than polygonal. Close to the antimesometrial pole of the embryo some of the cells have become involved in the degenerative changes taking place in the epithelial and subepithelial tissues (implantation zone of Krehbiel). This zone is surrounded by a narrow band of uninuclear cells which is the primary decidual zone, now much reduced; outside that is an annulus of very tightly packed cells, many of them binuclear, and many more in mitosis. These nuclei are large, and usually demonstrate two distinct nucleoli. The cytoplasm stains lightly with eosin, and is very finely granular. The capsularis is bounded and separated from the circular muscle by a narrow strip of almost completely unchanged uterine stroma (Krehbiel's basal zone) in which the remains of the compressed glands of the resting uterus may still be seen. The line of demarcation between the capsularis and the basal zone shows a layer of flattened decidual cells, orientated parallel to this line and staining somewhat more deeply than the rest. They increase in number and prominence in later stages.

The second and third zones, comprising together the "decidua basalis" (Duval's "caduque serotine"), are equivalent respectively to Krehbiel's "central area of the mesometrial region" and "glycogenic area and sinusoids". The chief distinction

between the two zones at this stage is that the narrow, third zone has prominent vacuoles in the cells and contains large sinusoids; later the second zone also takes on these characters and the whole of the basalis becomes uniform in appearance. The cells of the basalis do not show so marked a change from the parent stromal cells, when compared with the cells of the capsularis. They are fairly compact, especially around the implantation pit, where they are flattened parallel to the long axis of the pit (Jenkinson's layer of vacuolated and flattened cells, labelled "v.f.c." in his diagrams). The nuclei are large, with a distinct nucleolus, and the cytoplasm is scanty, clear and slightly basophilic; as already pointed out, cells with the prominent vacuoles indicative of glycogen formation have appeared in the most antimesometrial part of the basilis (Krehbiel, Fig. 1E). The uterine lumen and, in particular, the implantation pit are now very narrow; the latter exhibits three regions, more or less corresponding to the three zones previously described (Fig. 3). The one remote from the mesometrium contains the embryo (Z_1), and the cavity and epithelium of this part have been obliterated by its expansion. The intermediate region has almost completely lost its epithelium, which has been shed into the lumen (Z_2). Here it has mingled with some decidual cells and with blood which has leaked out of the sinusoids nearest to the epithelium, to form a coagulum—the maternal symplasma. The region nearest the uterine lumen retains its epithelium, which is still of a low columnar type, like that of the adjoining lumen (Z_3).

The vascular changes show a distinct advance on the previous day (see diagram). Whereas the capsularis is relatively avascular, showing very few vessels other than capillaries, the basalis is riddled with venous sinusoids, which are largest in the adjacent glycogenic zone (Fig. 4). The arteries which pierced the circular muscle directly from the mesometrium in the barren uterus are visible again, especially at the level of the implantation pit. At first they pursue a coiled course through the basalis, but then become straight, and bifurcate close to the degenerating papilla previously described (Figs. 5 and 6). At this stage these arterioles have a diameter of 15–20μ. The two branches pass around the uterine lumen, and join the much increased subepithelial plexus bordering the implantation pit. From this the blood passes laterally into the veins which formerly drained this plexus, now dilated into sinusoids scattered throughout the basilis, especially the glycogenic portion, they eventually drain into the veins lying against the circular muscle; and thence into the uterine veins in the mesometrium. The veins within the uterus often form a "collar" or "halo" around the ingoing arteries, and, in both injected and non-injected specimens, show leakage of blood (or ink) into this basal, outer part of the decidua basalis. It may be noted that the implantation axis, i.e. the line of the incoming arteries and the implantation pit, rarely passes through the middle of the attachment of the mesometrium to the uterus, but invariably to one side or the other of it (Diagrams I and II). Thus, it would seem that implantation is not strictly antimesometrial, but slightly lateral, although only in very small degree.

As already mentioned the capsularis is very poorly supplied by blood in comparison with the basalis; the only vessels seen are capillaries winding amongst its packed cells. These are fed by a few small arteries piercing the circular muscle obliquely from the antimesometrial side of the uterus, and traversing the unchanged basal zone to reach the capsularis. Most of them drain into the nearest sinusoids of

the basalis; few veins, or venules, can be seen leaving the capsularis.

Both in the sinusoids of the basalis and the capillaries of the capsularis, leucocytes are present in relatively large numbers; in the former they mostly lie close to the walls of the vessels. Some leucocytes lie free amongst the cells of the capsularis. These observations suggest that the circulation through the uterus at this stage is slow and sluggish.

Ninth day. The decidua capsularis shows relatively little change from the previous day; it is now clearly demarcated from the basal zone without and the embryonic cells within by the layers of flattened elongated cells before mentioned, and the region of transition to the glycogenic area of the basalis is now quite abrupt. The embryo, however, has made great advances; it has increased considerably in size. The ectoplacental cone (Duval) or Träger is well formed and prominent. The cavities of the ectoplacenta and amnion are quite distinct from each other, but still in communication by a narrow neck across the exocoelom (see Diagram II and Grosser (1927, Fig. 131)). The bud of allantoic mesoderm protrudes into the exocoelom. The yolk-sac presents visceral and parietal walls (proximal and distal of Duval) and around these Reichert's membrane (Duval's "cuticule ectodermique") and the layer of giant cells, variously called the "central zone" (Everett, 1935), the "cellules ectodermiques géantes" derived from the "ectoderme distal" (Duval), and the "Durchdringungszone" (Grosser, 1927). The first blood islands can be seen in the splanchnopleure of the yolk-sac wall. The cells of the central zone, immersed in maternal blood which has leaked into this part of the implantation pit (Duval's "cavité de la caduque") are of two types. The more numerous are relatively small cells, with pale cytoplasm, dark nucleus and rounded cell body. The remainder, few in number, are typically giant cells; both cell-body and nucleus are large, the nucleus is granular, and the cytoplasm presents angular, outstretched processes suggesting the possibility of amoeboid action. Most of these giant cells are closely applied to the decidua.

The Träger presents the appearance of a sharp-pointed cone, with an outer layer of giant cells adjacent to the maternal tissues, and within this its syncytial mass or ectoplacental cone, together with the distinctly cellular part bounding the ectoplacental cavity. The apex of the "cone" is thrusting into the mass of symplasma and blood in the implantation pit, and already lacunae containing maternal blood can be seen within it (Fig. 7). The vacuolation, indicating the presence of glycogen, has spread further mesometrially in the basalis, so that about half now presents this appearance. The uterine lumen is markedly reduced, the epithelium surrounding it is still intact, whereas all that lining the implantation pit has disintegrated and, in the cavity of the pit, mingles with the blood which has leaked in from underlying sinuses, some of which have probably ruptured spontaneously, others due to the ingress of the Träger. The latter is advancing along the line of the pit, now marked by a broad streak of symplasma, disrupting this and eroding adjacent sinusoids in the process.

The vascular arrangments delineated in the previous stage are now clearly marked (Fig. 7). Two or three prominent arteries pierce the circular muscle at the mesometrium, and run up to the uterine lumen before bifurcating, whilst the other arteries supply the outer part of the decidua basalis. Apart from these special arteries mesometrially, all others within the ring of the muscular coat have disappeared. Already in the former the first signs of the cells generally called "swollen endothelium"

can be seen. Whether these cells are really endothelial, or of a decidual origin, replacing the true endothelium, is uncertain, for similar reactions may be observed in scattered decidual cells in the close vicinity of the vessels. However, the early onset of this phenomenon, definitely under way at the next stage, suggests that the cells are unlikely to be derived from embryonic sources, for they are appearing at distances at present considerably removed from the nearest embryonic cells of the Träger. This view is at variance with that of Pritchard (1947) who believes the "swollen endothelial" cells in the metrial gland region to be of foetal origin on account of their high alkaline phosphatase content. On the 11th day, however, he speaks of the endothelium of the maternal blood-vessels in the basalis as being stained intensely by Gomori's method for phosphatase. It is not clear from his account that adequate distinction is made between the "swollen endothelial" cells of the maternal vessels and the cells of the trophoblast which line the central "artery" of the placenta from about the 12th day till term. These swollen cells clearly delineate the arteries, which are by now about 35μ in diameter. The sinusoids are greatly increased in number and size, particularly near the Träger; many of them have ruptured, releasing blood into the symplasma and into the lacunae of the Träger. The capsularis is slightly more vascular, as its capillaries are somewhat larger. It is quite easy to discern that a number of them communicate with, and discharge their blood into, the spaces of the central zone, as the sinusoids release their blood amongst the giant cells overlying the Träger, which are directly continuous with those of the central zone. The distant endothelium of these capillaries ceases abruptly where they open into the central zone. In all the injected specimens of this stage the central zone is considerably distended and the cells widely separated (Fig. 7). The area contains large quantities of maternal blood, with little Indian ink. In spite of what may happen in later stages (see Everett, 1935), this suggests that at present there is no circulation of blood among the cells of the central zone, it having seeped in from ruptured vessels, as it does into the Träger and into the trophoblastic lacunae in the human. Probably the injection pressure has been fairly uniform throughout most of the vessels, and so almost certainly higher than the normal blood pressure here. As a result, much blood, followed by some injection mass, has been driven into the central zone by the pressure, from which it cannot escape as the circulatory pathway has not yet been established; hence, it has accumulated here, and caused swelling of the central zone. Later, when a circulation has been established, this does not occur. Leucocytes are still present in considerable numbers in most vessels.

Tenth day. The uterine lumen is now showing the first signs of re-establishing itself on the antimesometrial side of the uterus (Fig. 8 & Diagram III). This takes place by a splitting of the line of junction between the basal zone and the layer of flattened cells bounding the decidua capsularis, the former forming the new layer of uterine stroma on the antimesometrial side of the uterus. Sometimes a very thin layer of the stroma of the basal zone remains on the decidua; although uterine epithelium covers over the basal zone at once, it never clothes the capsularis. The latter is now decidedly thinner than before, largely due to mechanical distension by the embryo. At its junction peripherally with the basalis, the glycogenic vacuolation has extended into it for a short distance, and the venous sinusoids have extended into the same area.

The body of the embryo is now formed. The neural tube shows the brain vesicles,

and has closed in the mid-dorsal region, although still open anteriorly and posteriorly. Heart and pharynx are well developed, but the mid-gut is widely open to the yolk-sac. Limb buds are present and there are many blood islands on the yolk-sac. The ectoplacental cavity has been obliterated, and the allantoic mesoderm just comes into contact with the underside of the ectoplacental cone ("lamina" of Everett). The cone has now broadened its base, so that relative to the previous stage it appears flattened; nevertheless, it has continued to extend in a mesometrial direction.

Almost all the basalis is now vacuolated. It is difficult to find traces of the old uterine lumen which formerly passed through this region. The incoming arteries are distinct, and generally there are two main ones to each placental region. Although, for convenience, the term "artery" is retained for these vascular channels throughout this account, the sole justification for this usage from this stage onwards is the direction of flow of the contained blood, for they lose all trace of an arterial or arteriolar wall, and become increasingly voluminous. In these arteries, whose average diameter is about 50–55μ, the "endothelial" reaction is now distinct, particularly in their terminal portions; the cells are large and round and the cytoplasm stains a peculiar glassy pale blue in haematoxylin and eosin sections (Figs. 9 & 10). In the terminal parts of the arteries they form a complete wall, but in the outer, coiled, parts they alternate with areas of apparently normal endothelial cells. According to Selye and McKeown (1935) these cells are endothelial, but are a part of the nutritional complex formed by the decidua basalis and the myometrial gland for the nutrition of the embryo and are shed into the lumen of the arteries. This suggests that they may be the same as the maternal glycogenic cells which Jenkinson (1902) describes floating free in the placental lacunae. No observations have been made upon this point. The trophoblastic giant cells of the Träger are now approaching the site of the old uterine lumen, and have virtually reopened and occupied the implantation pit in its mesometrial half. Consequently, instead of running parallel to each other as before (Diagram I), the branches of the arteries now diverge approximately at right angles, and pass along parallel with, and close to, the margin of the giant cells (Diagram III). As a result the sinusoids come to be directed towards the mesometrium rather than laterally; the appearance of the maternal circulation, as seen in a transverse section, suggests a "fountain" arrangement, with the blood passing straight up the arteries in the centre, and then in a cascade outwards and downwards towards the uterine veins. A considerable amount of maternal blood is incorporated in the trophoblastic part of the placenta, and, judging by the quantity of injection mass found amongst the cells of the central zone, the blood is beginning to circulate freely through the area.

Eleventh day. The decidua capsularis is considerably attenuated, and the uterine lumen around it is almost completely re-established. The thickness of the central zone, i.e. from Reichert's membrane to the inner face of the capsularis, is unchanged. The cells in the central zone have all been converted into giant cells.

The Träger has broadened even further and the inversion of its margins is quite evident, carrying with them a part of Reichert's membrane and the distal wall of the yolk-sac on to the embryonic face of the placenta, with the resultant formation of an entodermal sinus. The apex of the ectoplacental cone has become rounded off, so that the trophoblastic cells are assuming the form of a flattened mass. Consequently, the decidua basalis is partially divided into

two halves along the line of the old implantation pit; these have been "splayed" apart by the invasion of the foetal part of the placenta, so that the interface between the trophoblastic giant cells and the decidual cells runs more or less transversely across the uterus, presenting a convexity towards the mesometrium (see Grosser (1927, Fig. 135)). The allantoic vessels and mesoderm are commencing their invasion of the ectoplacenta from the foetal side, and from now on it is possible to divide the foetal placenta into three parts. First, the labyrinth nearest the foetus which contains both maternal and foetal blood streams; outside that, the plasmodial reticularis, which later becomes glycogenic, and is never vascularized from foetal sources; finally, abutting on the maternal tissues, a layer of giant cells. Duval, whose observations were made chiefly on the mouse, states that the original layer of giant cells covering the ectoplacental cone is pierced by its expansion, and thrust laterally on to its sides, and that later a second generation of giant cells is formed from the underlying reticularis. In the present preparations of rat uteri, giant cells occur on the outside of the foetal placenta throughout term, although they are, in later stages, few in number, much flattened and attenuated. At this stage they are actively engaged in the invasion of the maternal sinusoids surrounding the main terminal branches of the maternal arteries (Fig. 11) and incorporating them within the foetal placenta.

The maternal arteries are further increased in diameter, to about 75μ. However, in the straight terminal part of their course, near the trophoblastic cells, the lumen of the vessels is almost completely obliterated by the swollen "endothelial" cells. The basal outer portions of the arteries are still somewhat coiled. Because of the lateral displacement of the decidua basalis, their main terminal branches run almost transversely across the uterus, just within the foetal part of the placenta, and the general direction of the sinusoids is now towards the mesometrium; they are thus becoming parallel with the arteries, but the blood streams in the two sets of vessels are opposite. Thus the pattern of the maternal placental circulation is clearly indicated and it can be seen that it will conform to the pattern already described in other animals.

Twelfth day. The uterine lumen has completely re-established itself on the antimesometrial side of the uterus. The decidua capsularis is extremely thin, and degenerating throughout, the cells being strongly eosinophilic. In places the central zone is almost exposed to the lumen. It is now a compact layer of giant cells, amongst which maternal blood circulates, in direct contact with the outer surface of Reichert's membrane. Everett's (1935) work would indicate that it is a rapid circulation, and that it takes an important part in the nutrition of the embryo at this stage. The embryo has developed pharyngeal pouches and a lens pit. The optic vesicle has partially invaginated to form the cup, but there is still a distinct cavity left, which is continuous with the cavity of the brain through a widely open optic stalk. Villi and folds now appear on the proximal wall of the yolk-sac, especially near the allantoic placenta. In the labyrinth, the main "villi" of allantoic mesoderm, with their foetal vessels, are well developed, and the labyrinth and labyrinthine circulations definitely established. These villi are already arranged in a radiate manner, centring on the attachment of the allantoic stalk or umbilical cord to the inner face of the placenta.

The basalis has entered upon its state of decline. It is reduced in thickness, partly due to further invasion by the trophoblast, but also to some extent by a diminution of its glycogen content, as indicated by decreased vacuolation.

In some of the injected specimens at this stage it is only possible to identify one big maternal placental artery. The maternal arteries now terminate within the labyrinth of the placenta in two or more large sinus-like branches which radiate outwards. These arteries are coiled in the mesometrium and in the developing "myometrial gland" tissue, but become straight as soon as they penetrate the rather loosened and indistinct layer of circular muscle. The part of the artery within the foetal placenta is rather wider than that not yet incorporated and has a diameter of about 125μ. It has lost all its "swollen endothelium", and is lined simply by cells of the trophoblast, as are all the maternal blood spaces in the foetal placenta. The reaction of the "endothelium" however, has spread to involve those parts of the arteries within the mesometrial zone of attachment to the uterus, amongst the metrial "gland" tissue ("insertion zone" of Selye and McKeown).

As mentioned above, the arteries bifurcate and pass over laterally into large sinuses within the placenta. These sinuses deliver their blood into the maternal blood spaces in the labyrinthine part of the placenta, through which the blood percolates towards the mesometrium, emptying eventually into the uterine veins. A prominent feature in injected specimens of later stages is the pool of maternal blood surrounding each of the main allantoic "villi". These maternal blood spaces are derived from the big sinus-like branches of the arteries, and the blood in them flows through the placenta around these main villi into the sinusoids in the reticularis and the basalis. Hence, the flow of this maternal blood is parallel with, and in the same direction as, the flow of the blood in the arteries of these main "villi"; consequently it must be opposite in direction to the foetal blood which passes out of these arteries into the foetal capillaries and flows back towards the radicles of the umbilical veins at the attachment of the umbilical cord to the placenta.

Thirteenth and fourteenth days. At this stage the distal, or parietal, wall of the yolk-sac together with what remains of the decidua capsularis commences to disintegrate. The capsularis is little more than a syncytial sheet of degenerate cytoplasm in which the nuclei of the cells remain embedded. The central zone, likewise, is very much thinner than heretofore, but still contains an appreciable amount of maternal blood. Reichert's membrane is very distinct and appears to be intact in all except one specimen. Blood (or ink) is seen in the uterine lumen in the 14-day specimens and comes from the central zone through the capsularis, particularly near the margins of the definitive placenta, where the blood sinuses in the central zone are larger and looser. This is in essential agreement with Stafford's (1930) observations on the origin of the blood of the "placental sign" of Long and Evans (1920). The vitelline epithelium on the proximal wall of the yolk-sac now shows well-formed villi, especially where it faces the inner surface of the placenta.

The re-established uterine lumen is beginning to undermine the margins of the placenta, by splitting the decidua basalis. The newly formed uterine epithelium which clothes the wall of the new lumen is folded, and the cells are tall and finely vacuolated. The underlying stroma is very vascular and the glands have re-formed.

In the placental area, the decidua basalis, considerably reduced, has lost most of its glycogen and is clearly degenerating. The distension of the uterus by the growing foetus, however, has caused great thinning of the muscle coats; over the mesometrial area the circular muscle has become much broken up and hard to define as a layer by

the formation and development of the "myometrial gland". The "gland" tissue thus is more or less continuous with that of the decidua, and resembles the decidua basalis of the earlier stages, as its cells are commencing to show the glycogen vacuoles. The foetal part of the placenta has further increased in size and more than half its bulk is formed by the labyrinth. The reticularis is also beginning to accumulate glycogen but shows little increase in thickness as compared with former stages. The giant cells form a very thin and compact, but apparently continuous, layer. The cells have become rather spindle-shaped, because of tight packing. Both nucleus and cytoplasm are pale; the nuclei show one or two nucleoli. The maternal arterial channels are considerably increased in dimensions, possessing a diameter of about 200μ (Fig. 12). These arteries, one or two in each placenta, are quite straight, and extend right through its whole thickness to terminate in a subchorial position; here they give rise to two or three sinuses, almost as large as the parent arteries, which radiate laterally, also in a subchorial position, and dwindle away by giving rise to the prominent blood spaces around the main villi of the placenta. The entodermal sheaths of these villi, which Duval described (his "entoderme ectoplacentaire" derived from the "sinus entodermique"), can be seen clearly, becoming more and more prominent towards term. Apart from these main maternal blood channels, all the large lacunae and sinusoids of the previous stages have been broken up by the trophoblast, thus forming the most intricate maze in the labyrinthine part of the placenta. The foetal vessels are beginning to contain mature non-nucleated erythrocytes.

In the decidua basalis the sinusoids which are draining the placenta and emptying the blood into the uterine veins are large and numerous, honeycombing the decidua, but they appear compressed and slit-like on section. At this stage the reticularis is virtually free from large sinusoids. In that part of their course through the myometrial gland the placental arteries still show a distinct "endothelial reaction", but elsewhere this has disappeared. The fully developed placental circulation has been established. The course of the maternal blood through the channels of the labyrinth is from the foetal to the maternal side, whereas the blood in the foetal capillaries flows from the termination of the allantoic arteries on the maternal side of the labyrinth towards the umbilical veins in the body stalk. Thus, the flow of the foetal and maternal blood streams is in fact parallel and opposite in direction, and the whole pattern and arrangement corresponds closely to that in the rabbit described by Mossman (1926). Further changes are largely an elaboration and increase of the extent of this condition, and, later, are directed towards the detachment of the placenta at the termination of pregnancy.

Fifteenth and sixteenth days. No great changes occur in this stage, but the processes already seen in the early periods of development continue. The distal wall of the yolk-sac has ruptured and retracted to the margin of the placenta, forming a "zone résiduelle" (Duval), in which the thickened remnant of Reichert's membrane can be distinguished. Thus, the cavity of the yolk-sac becomes directly continuous with that of the uterus, and the epithelium of its proximal wall lies against that of the uterus. The villi on the yolk-sac become more highly developed, and reach relatively great lengths on that part of the vitelline epithelium which abuts on to the foetal aspect of the placenta.

The decidua basalis is reduced to a very narrow and compact layer, except for a thicker collar of tissue around the maternal arteries. The labyrinth is further elaborated

and extremely vascular, being a vast honeycomb of blood from both sources. The maternal arteries are increasing rapidly in size; in the 16-day specimens, only one artery, as a rule, can be discerned (Fig. 13). It is uncertain whether this is due to coalescence of the two arteries present in earlier stages, or disappearance of one of them. The former is more likely since these "arteries" are in reality only large blood channels through the trophoblast, with no real walls of their own. The large, slit-shaped sinusoids which lay in the decidua in the previous stage are now being surrounded by the giant cells and coming to lie in the reticularis, which contains much glycogen; thus, all parts of the maternal circulation, right up to the venous channels which pass through the circular muscle into the uterine veins in the mesometrium, are now within the foetal placenta. In these sinusoids free cells can be seen floating; Jenkinson (1902) has claimed that these are maternal glycogenic cells. Frequently small groups of giant cells can be seen lying just within the reticularis, the expansion of which cuts them off from the surface of the foetal placenta.

Seventeenth and eighteenth days. By the close of this stage the placenta has attained its maximum size and development. Both the reticularis and layer of giant cells are beginning to be reduced; the former is losing its glycogen and shrinking, the latter becoming very thin and incomplete (Diagram IV). In the labyrinth, the trophoblastic cells are becoming flattened, and spread out upon the walls of the foetal capillaries in the form of cytoplasmic plates with prominent nuclei, thus giving rise to the appearance of the haemo-endothelial type of placenta (see Mossman, 1926, 1937; also Bremer, 1916). The "villi" bearing the foetal arteries are very large and both the contained arteries and the entodermal sheaths are prominent. They extend to the junction of the labyrinth and reticularis. The foetal red blood cells are adult in appearance.

The maternal artery (again generally only one at this stage) is a voluminous structure, and has attained a diameter of 1 mm., or even more, on the 18th day (Fig. 14). It can be seen easily by the naked eye in the sections of the uninjected as well as the injected placentae.

The process of separation of the placenta from the uterine wall by the re-formation of the uterine lumen has proceeded apace, and the placenta now lies virtually free in the uterus, attached to the mesometrial part of the uterine wall only by a broad pedicle formed of the remains of the decidua. This process of separation of the placenta from the uterus occurs at such a plane that all the large venous spaces lie on the placental side of the cleft, amongst the giant cells and the outer part of the reticularis. These coalesce to form a circular venous sinus around the outer, maternal aspect of the placenta, draining all the maternal blood from the placenta, and in its turn emptying into the uterine veins in the mesometrium, through the "pedicle" around the artery. At the margins of the placenta there is an area involving the giant cells and part of the reticularis undergoing hyaline degeneration. This increases considerably towards term.

Nineteenth and twentieth days. This final period does little more than show an elaboration of the processes at work in the previous stage. Almost the whole bulk of the placenta is formed by the labyrinth. The reticularis, very much reduced and shrunken, has given place to the annular venous sinus already described. However, it is somewhat thicker at the margin of the placenta and it also persists as a sheath around the maternal artery through most of its course within the labyrinth (Fig. 15). Islands of reticular cells can be seen in-

corporated within the labyrinth; the giant cells, likewise, have almost disappeared except at the lateral edge of the placenta.

The " pedicle " attaching the placenta to the uterine wall is still narrower and contains almost all that remains of the decidua. At this point the artery shows a slight constriction but elsewhere is undiminished with no other signs as yet of occlusion in preparation for the impending parturition (Fig. 16). In one injected 20-day placenta, which still presented two arteries, a third channel resembling an artery, but smaller, lay between them. This channel passed vertically through the placenta, and communicated with the venous sinuses draining it within the pedicle. This would seem to be an anomalous venous channel draining some of the maternal blood. This observation may help to explain Duval's repeated statement that the large central vessels of the placenta are efferent, i.e. they are venous, transporting maternal blood *away* from the placenta. This is not the usual arrangement.

In conclusion it will be seen that at implantation the earliest vascular changes in the rat's uterus consist of sinusoidal dilatation of the capillaries and veins of the endometrium with but little reaction on the part of the uterine arteries. This at first is mainly limited to the glycogenic zone of the decidua basalis, and both sinusoidal dilatation and the glycogenic zone develop *pari passu*. This stage is reached about the 10th day of pregnancy, by which time the uterine lumen is being re-established in the region of the decidua capsularis, which has exhibited throughout this period a much less intense vascular reaction than the decidua basalis. At this stage small groups of radially running arteries on the mesometrial side of the uterus opposite each implantation pit commence to dilate and become conspicuous, whilst the Träger occupies the whole implantation pit and approaches the old uterine lumen and the site of bifurcation of these arteries.

From the 10th day onward the phenomena which lead to the establishment of the final vascular relations within the placenta proceed rapidly. These consist of broadening of the Träger, leading to opening out of the implantation pit and splaying of its walls laterally and toward the mesometrium; of progressive replacement of the decidua basalis by trophoblast which also invades the sinusoids in this region, the maternal blood channels, both arterial and venous, becoming incorporated within the foetal part of the placenta. These blood channels lose their original walls and become bounded everywhere by foetal tissue. The original two or three radial arteries supplying the placenta thus merge into a single large central channel, the branches of which pass laterally and horizontally as large sinuses in a subchorial position. From these the blood drains backwards along the main villi and towards the mesometrial half of the uterus. It is also at this stage that the foetal portion of the placenta becomes vascularized from allantoic mesoderm.

These processes proceed until about the 17th or 18th day, when the placenta has attained its maximum development. Meantime the new uterine lumen, re-established on the antimesometrial side at the 10th day, has progressed towards the mesometrial side, undermining the placenta and leaving this attached to the uterine wall by a progressively narrowing pedicle through which pass the main maternal vascular channels supplying and draining the placenta. This process is clearly in preparation for the impending parturition, as is the narrowing and enhanced irritability of the artery entering the placental pedicle.

The Sheep.

Barcroft and Barron (1946) have studied

the form and arrangement of the circulations in the placenta of the sheep, correlating changes in the gaseous tensions of the blood of the umbilical veins with the changes in the disposition of the foetal and maternal vessels. In so far as the established placenta is concerned there is nothing to add to their account, but their description of the vascular condition in the barren uterus and the mode of early penetration of the foetal villi into the uterine burr is open to criticism.

The material used consists of sheep foetuses and uteri from an abattoir and contains many specimens of a later age than those listed in Table I. Great difficulty has been found in maintaining the foetal membranes in contact with the uterine wall while the blocks of tissue were being impregnated with celloidin, and even preliminary embedding in gelatin has not been completely successful in overcoming this difficulty. However, the observations are not invalidated by this fact.

The tentative copulation ages awarded to the various stages are based on the table in Assheton's monograph on the sheep placenta (1905, p. 207), to which work Barcroft and Barron make no reference.

The non-pregnant uterus. The uterus which contains a free blastocyst will also be considered under this heading as it presents no fundamental or important changes from the barren state. On all significant points save one the observations tally with those of Bancroft and Barron, and so the conditions obtaining in the uterine burr or cotyledon alone will be discussed. The uterine vessels to the burr are large, prominent, and arranged in spirals in the tissue between the uterine muscle and the base of the burr proper. From the arteries, a number of branches arise which form tight " corkscrew " spirals running into the base of the burr, where they in turn often subdivide further into two or three branches (Fig. 17). The stroma of this part of the cotyledon is especially dense, and as they pass through it, the arteries lose the greater parts of their coats, and are difficult to see when not injected. They run straight towards the inner free surface of the cotyledon, and, as Barcroft and Barron point out, appear to be constricted and might better be called arterioles. They give off very few, if any, branches as they pass through the cotyledon until, when nearly at the epithelium, they break up into a spray of relatively large capillaries. These form a dense network of blood-vessels in the subepithelial stroma, which is most loose here, and many capillaries appear to contact the bases of the epithelial cells of the mucosa. A small number of arteries also enter the cotyledon at its periphery from the glandular part of the uterus. The capillary loops, turning back on themselves, gradually unite to form veins at about the junction of the superficial and middle thirds of the burr; these are more voluminous than the arteries, and pass out into the large uterine veins underlying the burr. No trace of the venous sinus described by Barcroft and Barron as immediately underlying the uterine epithelium has been seen in any of these specimens. Even the specimen of early pregnancy only shows a general dilatation of the vessels in the burr and under the epithelium. Although Barcroft and Barron (p. 579) say that " Immediately beneath the basement membrane of the epithelium there is a very rich venous plexus, amounting to a sinus, which covers virtually the entire cotyledonary surface ", and illustrate this [Plate 1, Fig. 3], in their summary (p. 591) they make no mention of a sinus and speak only of a subepithelial capillary plexus, as described here. As will be seen later this so-called " sinus " is probably an artefact. Assheton (1905) and Marshall (1903) make no reference to any such

structure, which, having a depth of more than 200μ, would probably be noticed even in uninjected specimens. According to Barcroft and Barron, this sinus is invaded during implantation; it is unlikely that Assheton would have omitted mention of it in his close study of implantation if he had in fact seen it. Moreover, any epithelium which was floating directly on a lake of blood 200μ deep would be leading a very precarious existence and would be under constant threat of rupture with loss of appreciable amounts of blood into the uterine lumen.

Some observations of Marshall (1903) may help to explain the "presence" of this "sinus". During the period of pro-oestrus and oestrus in the sheep, the superficial subepithelial capillaries dilate and rupture into the surrounding stroma and sometimes even through the epithelium into the uterine cavity. His Plate 7, Figs. 3 and 4, illustrate these points. According to their list Barcroft and Barron had only one non-pregnant uterus in their series, possibly at this stage of the oestrus cycle, so that the injected mass passed out of the weakened and ruptured capillaries into the surrounding, relatively loose, uterine stroma, producing the "venous sinus". Their illustration appears consonant with this interpretation. The hydrostatic pressure by itself is unlikely to explain the anomaly; two barren uteri injected at a pressure of 250 mm. of mercury in order to test this point only showed some small scattered irregular ruptures, totally unlike the "sinus".

The pigment, although variable in amount and distribution, is usually very dense in the cotyledons, and largely concentrated in the layer of stroma just underneath the epithelium (Fig. 17); it also lies scattered in the middle depths of the cotyledon, especially around the vessels. Assheton differentiates this latter pigment from that more superficially placed, because of its lighter colour. Granules of pigment may also be seen in the epithelium. Marshall claims that the pigment is derived from the blood released from the capillaries during oestrus, but Assheton was unable to elicit a positive reaction for iron from it. Treatment of the sections with potassium permanganate and sulphurous acid bleaches the pigment to a very light brown, leaving the injected vessels showing more distinctly and indicating that the pigment may be allied to melanin.

10 *mm. Stage.* (*About twenty days old.*) The foetal membranes in both specimens are just commencing to invade the cotyledon; they have removed or displaced the epithelium and exposed the underlying stroma and capillary plexus. Only very occasionally, here and there, is there as yet an "erosion" of the stroma. There is no sign of any venous sinus, or of any ruptured vessels. The diplokaryocytes of Assheton are distinct, forming a discontinuous, irregular layer on the surface of the stroma. The views of Barcroft and Barron are difficult to reconcile with those of Assheton, who claimed that these diplokaryocytes, which persist to term, originate from the trophoblast. The "crypts" are probably artefacts due to shrinking of Wharton's jelly after fixation. Barcroft and Barron do not discuss this, nor do they consider the views expressed by Mossman (1937) on the fate of the uterine epithelium in the ungulate placenta, namely, that much of it persists to term.

Prominent in these sections is a distension of the veins, and a generally increased vascularity of the cotyledon. These cotyledonary veins commence to enlarge about a quarter of the way in from the surface of the cotyledon, but as many of the superficial capillaries are also dilated to the size of venules, the veins often appear to start right at the surface of the cotyledon, where they are exposed by the loss of the epithe-

lium. The deeper veins are irregular in shape and loosely and tortuously coiled, whilst at the periphery they tend to aggregate in bunches. They finally pass out of the cotyledon towards the midpoint of the base to drain into the underlying vessels of the uterus, which are also dilated. In the deeper parts of the cotyledon, there has now appeared a loose network of fine and incompletely injected vessels, mostly veins, not formerly visible.

The arteries have also dilated and become more distinct in the cotyledon, but not to the same extent as the veins. They, too, show enlarged terminal branches running right to the exposed surfaces. They are still straight and unbranched in the cotyledon, but as they enter the base, it can be seen clearly that they arise in leashes of two or three from coiled branches of the main arteries underlying the cotyledon. The latter has expanded, and presents a slightly concave face to the uterine lumen, so that now its margins appear curved up and undermined for some distance by the glandular tissue; the latter has not yet commenced to migrate over the sides of the cotyledon.

17 and 20 mm. (*About thirty to thirty-five days old.*) At this age the chorion is commencing to penetrate into the loose superficial stroma of the cotyledon; the "villi", if such they can be called, are very broad and the pits or crypts which they produce are shallow but wide. All the superficial capillaries are dilated and almost sinusoidal; some are quite devoid of any stromal or epithelial covering on that part of their circumference adjacent to the foetal chorion. However, despite this fact, there are very few ruptures of these capillary vessels; they do not undergo the process of disintegration of the surrounding stroma, but are "pushed aside" by the chorionic villi. There is no evidence that the villi are invading the veins or venous capillaries. Certainly, at this stage, the primordial villi have a considerably greater breadth than the veins. In the depths of the cotyledons, the arteries are relaxed and open, not tightly constricted as before. The endothelium, to which Barcroft and Barron refer, is still prominent; the coats of the larger arteries are somewhat thicker than before.

27 and 28 mm. (*About forty days old.*) These two specimens present a crucial stage; the villi have penetrated some distance into the cotyledon (about a fifth of its depth), although the membranes are still detachable. The most important changes involve the superficial plexus, which is now extremely prominent (Fig. 18). All the capillaries have dilated and become sinusoidal, and form a very close-meshed and dense plexus. Furthermore, this plexus has deepened to the same extent as that to which the adjacent villi have penetrated. In other words, both the villi and the dilated and increased plexus occupy just the same extent of the cotyledon in which they lie. The plexus shows a number of ruptures, mostly small, localized, and not necessarily bearing a close relation to the villi. Once again, the villi during their entry into the cotyledon displace the sinusoids laterally, rather than attacking them or the veins draining them. There does not seem to be any convincing evidence either at this or any other stage for the statement by Barcroft and Barron (p. 581) that "when the disintegrating has extended to a level which exposes the veins leading to the cotyledonary depths . . . the cavities of these veins are invaded by the villi".

Within the cotyledons, the arteries are now as prominent as the veins, and tend to be very slightly coiled in their basal portions (Fig. 19). Large arteries and veins extend right into the superficial plexus, where they are quickly lost amidst the

maze of sinusoids, to which their branches (or tributaries) contribute.

31.5 *mm.* (*About forty-five days old.*) This stage corresponds to Barcroft and Barron's four animals in the 43- to 48-day group, the earliest pregnancies listed in their table. The villi have rapidly expanded their depth of invasion, and penetrated nearly the whole thickness of the cotyledons, so that implantation is virtually accomplished. The pattern of the circulation is now as described by Barcroft and Barron. The arteries, large and quite distinct, run straight through the cotyledons toward the foetal surface, where they break up into capillary vessels. These arteries are always ensheathed in a layer of cotyledonary stroma, separating them from the foetal trophoblast; the capillaries lie in the stroma, forming a network around the whole length of the artery. The arteries contribute a number of side branches into this plexus as well as their main terminal branches. Near and around the tips of the villi, these capillary networks converge to form the veins draining out of the cotyledon. Apart from these basal veins, it is difficult to find any other veins within the cotyledon. Nevertheless, this is not due to villous invasion and obliteration of these veins. If the villi had grown down the veins, blood would surround the villi, and the veins in the uninvaded parts of the cotyledon would be in communication with the venous channels containing the villi. The histological picture of the cotyledon does not show any significant traces of extravasated blood round the villi, especially their tips, at any stage, apart from the later pools of blood around their bases, clearly described by Assheton, which appear only after implantation has been completed. Furthermore, the veins issuing from the cotyledon do not bear any very intimate relation to the tips of the villi, nor do they arise from the villous "crypts" which appear in the fixed specimens, probably because of the shrinkage of Wharton's jelly; instead, they arise from capillaries lying in the cotyledonary stroma between the tips of the villi.

The cotyledonary veins which have apparently disappeared are in reality incorporated within the sinusoidal network in the fully formed placenta. At the 10 mm. stage, a plexus of fine capillaries opens up throughout the cotyledon, so that there is a capillary network in its depths as well as the more prominent one at its surface; secondly, coextensive with the depth of invasion of the cotyledon by the villi, this deeper capillary network enlarges, expands and becomes sinusoidal (27–28 mm.), whilst the commencement of the veins within this network becomes inconspicuous. As the villi continue to penetrate the cotyledons, so the neighbouring small capillaries dilate to sinusoidal capillaries, and, as a result, the veins cease to be prominent and become a part of the network pervading the cotyledons, only their terminations draining out of the cotyledons remaining distinctly recognizable as veins. The distinction between capillaries and venules is lost, due to the sinusoidal dilatation of the former.

The Cat.

The non-pregnant uterus shows the same basic pattern as the cotyledons of the sheep and the uterus of the pig. The arteries lie, as in the rat, between the two muscle coats and are fairly tightly coiled. The veins are relatively small in the uterus and accompany the arteries for the most part. In this situation the latter give off radially-directed branches through the circular muscle running straight up to the epithelium. Here they break up into a capillary plexus which is then drained by small veins towards the muscle and into the main uterine veins. The endometrium is poorly vascularized, especially when com-

pared with that of the dog, which possesses the same pattern, but is much richer in blood-vessels. Our material fully confirms the observations of Tafani (1887) on the disposition of the vessels within the placenta. It consists almost entirely of foetal tissue; maternal tissues are represented solely by the vessels and by a thin layer, abutting on the uterine muscle, which consists largely of the dilated ends of the uterine glands. The maternal arterial channels, very large and straight, pass through this zone from the uterine arteries, and pursue a straight course towards the foetal surface of the placenta (Fig. 20). They are enclosed by a thick layer of trophoblast, which makes them very distinctive. About half-way through the placenta each of these arteries, previously running singly, divides into two or three branches (Figs. 21 and 22) which continue to the foetal surface in close proximity to each other (horizontal sections). Here, they turn at right angles to lie parallel with this surface, and run round the placenta at right angles to the long axis of the uterus and parallel to the borders of the placenta (Figs. 23 and 24). They lie close to the main foetal arteries, separated from them only by trophoblast. The foetal arteries also encircle the inner face of the placenta, parallel with the maternal ones.

Beyond their point of bifurcation, the maternal arteries continually give off side branches whilst travelling towards and lying immediately under the foetal surface of the placenta. All these vessels, most of them little bigger than capillaries, turn back towards the uterine wall, running parallel with the parent arteries to enter into a most complex mesh of capillary vessels. This is mainly disposed perpendicular to the surfaces of the placenta, alongside a similar arrangement of foetal vessels, so that a "horizontal" section of the placenta, i.e. one parallel with its surfaces, reveals a most intricate maze of alternating injected and non-injected capillaries, separated only by trophoblast.

Some of the branches of that of the artery lying under the foetal surface of the placenta are rather larger than the rest, and, after a very short course, open into small sinuses which lie near this surface. These "venous sinuses" are then drained by capillaries or venules which join the general capillary plexus. This arrangement is slightly reminiscent of Schlegel's (1946) description of "arteriovenous anastomoses" in the human endometrium, apart from the fact that the branches of the arteries in the cat, corresponding to his "arterioles" entering the sinuses, are much bigger, and possess no coats, other than a covering of trophoblast.

Near the uterine wall the capillary plexus collects into venules which drain into a number of irregular sinuses lying amongst the remnants of the uterine glands and thence into the uterine veins. As Tafani showed, the foetal vessels possess the same arrangement, i.e. the arteries run towards the maternal surface, and there break up into a capillary meshwork which drains in the reverse direction back to the foetus. Consequently, the blood streams in the capillary systems follow parallel but opposite courses. The foetal arteries are neither as large nor as prominent as the maternal ones, possibly because they possess well-developed coats.

A dog's uterus containing 30 mm. embryos shows a very similar pattern to that of the cat, though not, at that stage, so fully developed.

The Pig.

The pig possesses a very vascular uterus. The branches of the uterine artery pass to alternate sides of the uterine horn in a fairly regular series. As they encircle the uterine horn these arteries are tightly coiled

and lie at first immediately under the peritoneum, gradually piercing the muscular coats obliquely to lie in the endometrium, where they dwindle away on the antimesometrial side of the uterus. As they pierce the muscle coats, they give rise to a number of small arteries which run around the uterus for some distance between the muscular layers, which they supply.

From the main arteries a series of radial branches arise which run towards the lumen of the uterus, terminating in an exceedingly rich capillary plexus immediately underneath the epithelium (Fig. 25). This plexus is so dense that, to the naked eye, the celloidin sections (40μ) show a distinct, heavy, continuous black margin along the epithelial surface. This plexus is drained by an intertwined system of veins which present a widely branched arboreal appearance (Fig. 26). Radicles of these veins run for considerable distances under the epithelium and its plexus, receiving numerous small tributaries from the latter. These radicles then join to form the larger trunks, which pursue a meandering course to the main vessels, also coiled and tortuous, lying just within the muscle coats. Because of their widespread tributaries the territories of these veins draining the subepithelial plexus overlap to a considerable extent.

Around each gland there is a delicate capillary lacework, supplied and drained by small vessels, generally from the basal vessels. In the pregnant uterus the most outstanding change is a considerable, generalized enlargement of all parts of the venous circulation, with an increase in the superficial capillary net. The veins, distended and very prominent, are all coiled and tortuous, and the main basal ones are quite cavernous; some are irregularly valved. The early stages of pregnancy in the sow greatly resemble the conditions in the sheep and the arterial dilatation is insignificant as compared with that of the veins.

Discussion.

In the placenta of the rat and other mammals studied, the courses of the maternal and foetal circulations are parallel, but the direction of flow is opposite. As Mossman (1926) has postulated and Noer (1947) has demonstrated, this arrangement is best suited to an efficient interchange of diffusible substances across the placental barrier.

The maternal vessels in the uterus play a relatively passive part in the development of this circulation; the arrangement of the vessels in the non-pregnant uterus already presents the main features of the placental circulation. There, a capillary plexus underlies the uterine epithelium, supplied by arterial blood flowing towards the uterine lumen, and drained by veins whose blood flows outwards, parallel with but opposite to the arterial flow. When pregnancy supervenes, one or two chosen arteries enlarge to maintain the supply of the capillary plexus, while the rest soon disappear; the capillaries and veins dilate and are invaded and broken up to form a sinusoidal circulation by the foetal placenta. Thus the definitive maternal placental circulation is formed by the activity of the ectodermal trophoblastic cells of the Träger, the maternal blood channels playing a relatively passive role. To illustrate this, the length as opposed to the breadth of the maternal placental arterial channels has been measured in each specimen. The length of the vessels in the early stages so obtained is only approximate as they are coiled; the measurement has been taken from the inner surface of the circular muscle to the point of bifurcation close by the uterine lumen. Moreover, any slight obliquity in cutting the sections introduces an additional (small) error. Nevertheless,

allowing for these factors, fully developed arterial channels in the 18-day placentae are hardly any longer than the arteries of the 8-day stage from which they have been derived. Obviously, some contribution to their intra-labyrinthine extent must have been made in order to keep pace with the centripetal growth of the main mesodermal villi of the placenta, but this is barely detectable because of the crudity of the measurements. These observations indicate that after the earliest stages of pregnancy (i.e. after the 8th day) the maternal placental arteries hardly grow in length. The changes in their location, from lying entirely in the decidua basalis on the mesometrial side of the uterine lumen to being incorporated within the foetal placenta, terminating in a subchorial position, is not due to growth of arterial channels themselves, but to the activity of the trophoblast in surrounding and encapsulating these relatively static and passive arteries. The mode of invasion of the trophoblast by the vascular allantoic villi ensures that the foetal circulation in the placenta shall be parallel with but opposite in direction from that of the mother.

As a result, the pattern of the maternal circulation has an "umbrella" or "fountain" appearance — that is, the arterial blood "ascends" through the centre of the placenta to the foetal surface, where it radiates laterally, and "cascades" (through the labyrinth) on all sides, to be collected by the bigger venous sinuses on the lateral and maternal aspects of the placenta, and drained away. Duval's (1891) assertion that the central placental vessels of the rat and mouse are efferent, i.e., venous, is incorrect; in the arrangement of their placental vessels these two rodents correspond with other known members of that order. According to Wislocki and Streeter (1938), the platyrrhine monkeys resemble the rodents in the distribution of the maternal vessels in the placenta. Hill's (1932) description of the placental circulation in Tarsius also presents points of similarity to our studies, such as a large central maternal artery. Hence, the vascular pattern possesses a wide distribution in mammals.

Certain interesting changes, however, do take place in the maternal circulation at implantation. When implantation is taking place in the rat on the 7th day, the capillaries and veins dilate to become sinusoidal, whilst the arteries are difficult to see and, presumably, constricted and in spasm. The sheep resembles this at the 10 mm. stage. This condition of the circulation can be, and probably is, aided by the circular muscle, since it can, by its contraction, prevent both the ingress and egress of blood to the endometrium, without affecting the circulation through the main arteries outside this layer. This spasm of the arteries probably also occurs in the human, since it is very difficult to find them near the early implanted ovum (Ramsey, 1938), whereas dilated venules are quite noticeable. The restriction of the arterial blood flow with its reactive venous dilatation creates a stagnation of blood in the uterus, which condition the implanting ovum would seem to require. It means that when the superficial capillaries and sinusoids are ruptured, there will not be a considerable escape of blood under pressure, but a gentle percolation of blood into the lacunar spaces of the trophoblast; later, when the ovum is firmly implanted, the arteries open and a true circulation of the maternal blood through the trophoblastic region commences (about the 10th day in the rat, 27–28 mm. or earlier in the sheep); this is very easily demonstrated in the central zone of the rat's trophoblast, where at first the blood is not circulating, but merely infiltrating from the neighbouring ruptured capillaries. The number of leucocytes within the sinus-

KEY TO DIAGRAMS AND FIGURES.

A.—Artery.

A.L.M.—Allantoic mesoderm.

A.M.—Amnion.

C.M.—Circular muscle.

C.Z.—Central zone.

C.Z.M.—Central zone of the mesometrial region (Krehbiel).

D.C.—Decidua capsularis.

E.—Embryo.

F.V.—Foetal (allantoic) vessels.

G.—Uterine glands.

G.B.—Capillary plexus around a uterine gland.

G.Z.—Glycogenic zone.

I.P.—Implantation pit.

L.—Uterine lumen.

L.M.—Longitudinal muscle.

M.—Mesometrium.

M.U.—Muscle coat of uterus.

P.—Papilla.

P.S.—Placental venous sinuses (maternal).

P.Y.S.—Proximal wall of yolk-sac.

R.U.—Re-established uterine lumen.

S.—Venous sinusoids.

Tr.—Träger.

U.C.—Umbilical cord.

U.V.—Uterine veins.

V.—Vein.

Vi.—" Villus " of giant cells.

Y.S.—Yolk-sac.

Z_1, Z_2, Z_3—Zones in the implantation pit.

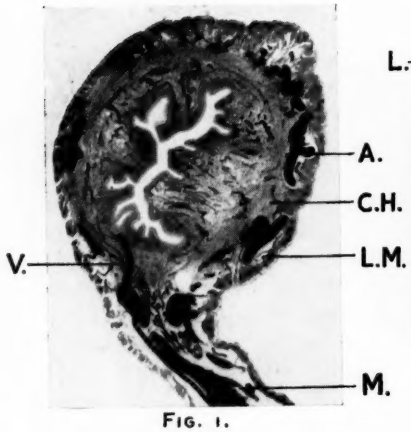


FIG. 1.

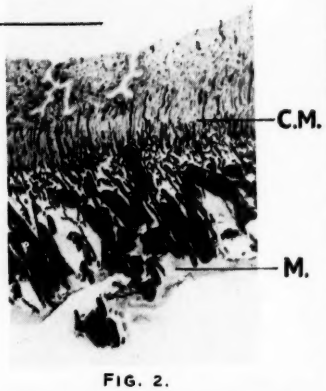


FIG. 2.

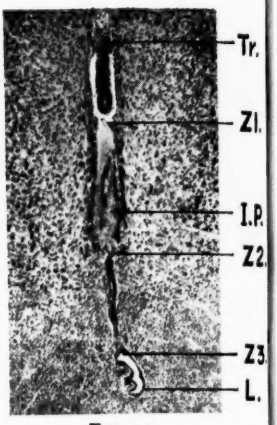


FIG. 3.

FIG. 4.

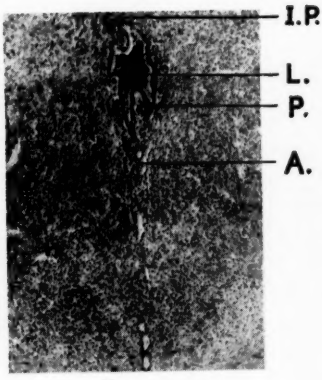


FIG. 5.

FIG. 6.

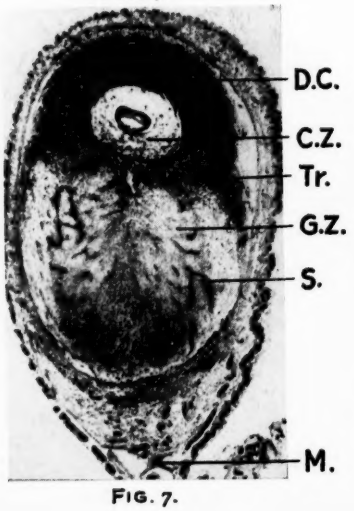


FIG. 7.

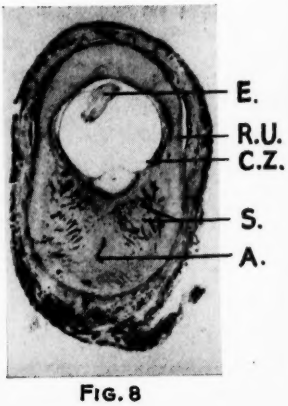


FIG. 8

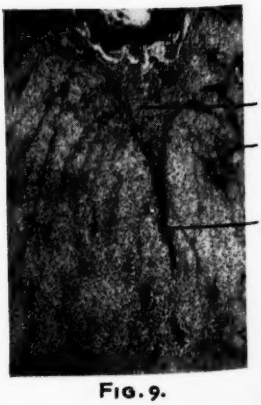


FIG. 9.

PLATE I.

FIG. 1—Transverse section of the uterus of a non-pregnant rat (R18); the vessels are injected with Indian ink. Note the spiral arteries between the muscle layers and the radially arranged branches passing inwards towards the uterine epithelium. A single large vein is shown draining from the basal part of the endometrium into the mesometrium. The extension of the longitudinal muscle into the mesometrium can also be seen. ×15.

FIG. 2—Sagittal section of the uterus of a non-pregnant rat (R18). This section has passed through the attachment of the mesometrium to the uterus. The vessels are injected with Indian ink and the radially arranged arteries passing inward towards the epithelium are particularly distinct on the mesometrial side. ×25.

FIG. 3—Section through an implantation pit on the 8th day of pregnancy in the rat (R22). Note the malorientation of the embryo and the zones (Z_1, Z_2, Z_3) described in the implantation pit at this stage. These zones are labelled at their mesometrial extremities. Stained with haematoxylin and eosin. ×30.

FIG. 4—Transverse section of the uterus of a rat (R22) on the 8th day of pregnancy. The section passes through the embryo and implantation pit. Note the venous sinusoids in the decidua basalis and glycogenic zone, and one of the radially coursing arteries (A) in the basal part of the endometrium. Stained with haematoxylin and eosin. ×12.

FIG. 5—Section of the rat's uterus (R22) on the 8th day of pregnancy, showing the degeneration in the papilla opposite the mesometrial extremity of the implantation pit with one of the radially coursing arteries of the endometrium approaching it. Stained with haematoxylin and eosin. ×45.

FIG. 6—High-power view of the degenerating tissue in the papilla facing the implantation pit on the 8th day of pregnancy in the rat (R22). Stained with haematoxylin and eosin. ×98.

FIG. 7—Transverse section of the uterus of a rat on the 9th day of pregnancy. The maternal blood-vessels are injected with Indian ink. The injected venous sinuses in the glycogenic zone of the decidua basalis are clearly shown, whilst the absence of injection mass from the central zone and its distension with maternal blood is significant. ×9.

FIG. 8—Section of the uterus of a rat (R11) on the 10th day of pregnancy. The maternal blood-vessels are injected with Indian ink. The uterine lumen is being re-established. The Träger shows further development and the ingoing maternal artery can be seen. The venous sinusoids of the basilis are being turned by the expanding Träger so as to be directed towards the mesometrium. ×6.

FIG. 9—Section showing the Träger and one of the maternal placental arteries in a rat (W283) at 10¼ days pregnancy. The branches of the artery and the venous sinuses are clearly delineated. Stained with haematoxylin and eosin. ×20.

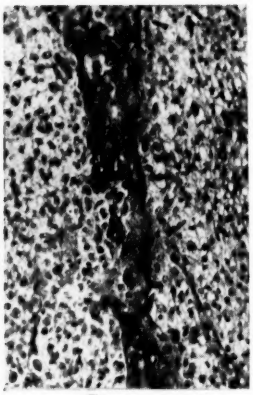


FIG. 10.

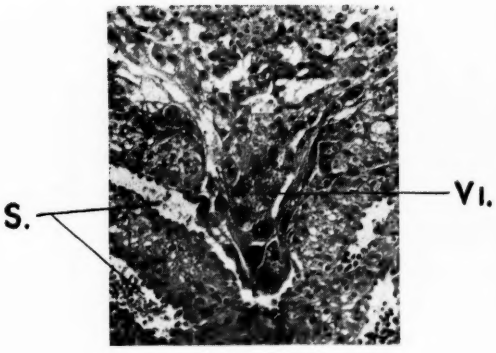


FIG. 11.

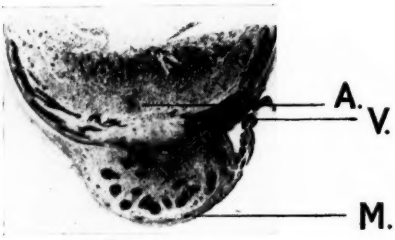


FIG. 12.

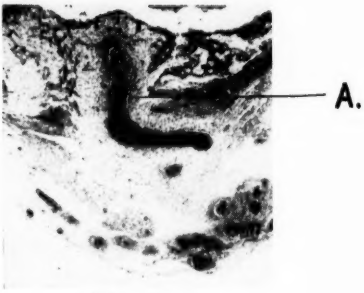


FIG. 13.

FIG. 14.

FIG. 15.

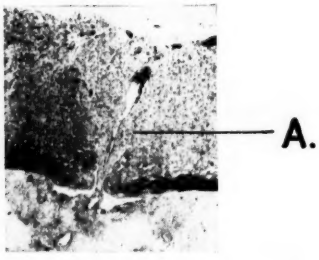


FIG. 16.

FIG. 17.

PLATE II.

FIG. 10—A high-power view of the wall of the artery seen in the preceding figure to show the endothelial reaction. Stained with haematoxylin and eosin. × 12.

FIG. 11—Section of the placental area in a rat (W277) at the 11th day of pregnancy to show the invasion of the venous sinuses by a " villus ". Stained with haematoxylin and eosin. × 98.

FIG. 12—Placenta of the rat on the 13th day of pregnancy. The maternal blood-vessels have been injected with Indian ink. Note the central artery (A) approaching the base of the placenta and the large vessels in the mesometrium, together with the venous sinuses draining the placenta. × 8.

FIG. 13—Central portion of the placenta of a rat at 16 days' pregnancy to show the central artery entering its base. The maternal vessels have been injected with Indian ink. × 14.

FIG. 14—Central portion of the placenta of a rat (R10) at the 18th day of pregnancy to show the central artery of the placenta. Note that the draining venous sinuses are directed peripherally from the foetal surface of the placenta. The maternal vessels are incompletely injected with Indian ink, and the injection mass has come out of the central artery (A) during preparation. × 6.

FIG. 15—Section of the placenta of the rat (R14) at 19 days. The maternal vessels and sinuses have been injected with India ink. This has been followed by a starch injection mass to fill the central artery (A). × 15.

FIG. 16—Section of the placenta of a rat (W296) at 19 days to show the narrowing of the central artery (A) as it passes through the muscle coat of the uterus to enter the base of the placenta. Stained with haematoxylin and eosin. × 10.

FIG. 17—Transverse section of a burr from the uterus of a sheep containing a free blastocyst. The blood-vessels have been injected with Indian ink. Note the spiral vessels at the base of the burr. The fine capillaries close to the free surface are obscured by pigment. × 6.

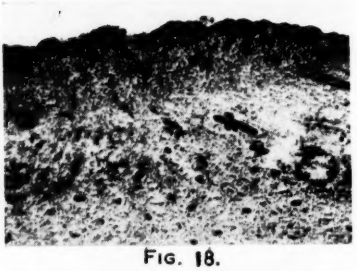
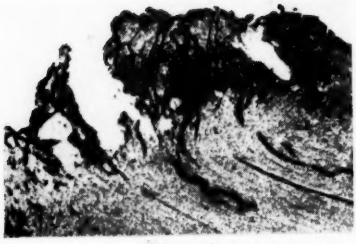


FIG. 18.



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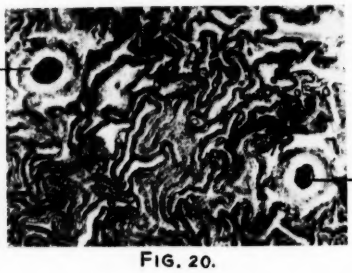

FIG. 20.

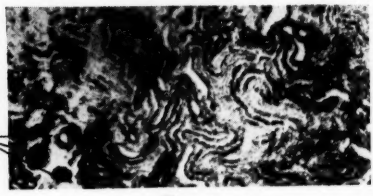

FIG. 21.

FIG. 22.

FIG. 23.

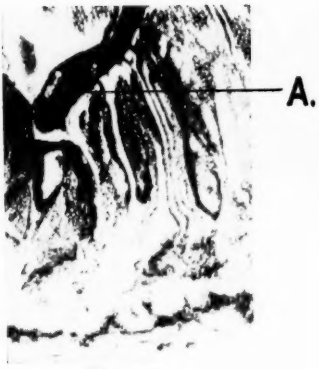

FIG. 24.

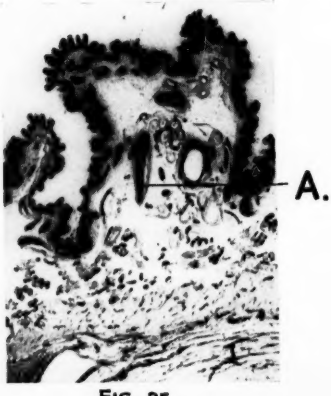

FIG. 25.

FIG. 26.

PLATE III.

FIG. 18—Transverse section through a burr from the uterus of a sheep containing a 27 mm. embryo. The maternal blood-vessels have been injected with Indian ink. The epithelium covering the burr has been destroyed and the chorion (detached from the specimen) has commenced to penetrate into the burr. Note the sinusoidal dilatation of the superficial capillaries. This specimen was taken from the tubal extremity of the uterine horn. ×38.

FIG. 19—Transverse section through one of the more central burrs in the same uterus as that shown in fig. 18. The foetal membranes have become detached but the excavations produced by the chorion are distinct. The further dilatation of the capillaries proceeding with the attachment of the membranes is shown and the lack of any extravasation of the injection mass into the uterine lumen is significant. ×38.

FIG. 20—Section of a cat's placenta near term. The plane of the section is parallel to the foetal surface and close to the basal part of the organ. The maternal blood-vessels have been injected with Indian ink. The main maternal arterial channels (A) are shown in section, coursing singly towards the foetal surface. The pattern of the maternal capillaries around the foetal trabeculae is also well shown. ×19.

FIG. 21—Section from the same placenta as and parallel with that shown in Fig. 20 but through the luminal half of the organ. The branches (A) of the arteries shown in the previous figure are clearly seen. ×18.

FIG. 22—Transverse section of a cat's placenta near term showing one of the maternal arteries (A) coursing towards the foetal surface and supplying capillaries and sinuses around the foetal trabeculae. The latter course backwards toward the uterine wall. The clear area on the main artery shows its site of bifurcation. The maternal vessels are injected with Indian ink. ×15.

FIG. 23—Section of a cat's placenta close to term parallel to and at the foetal surface of the organ showing a large maternal artery (A) running along the surface and giving its branches laterally and outwards to form the capillaries and sinuses around the foetal trabeculae. The maternal vessels are injected with Indian ink. ×19.

FIG. 24—Transverse section of the cat's placenta near term showing a maternal artery (A) turning to run parallel to the foetal surface of the organ and giving off its branches backwards towards the uterine wall. The maternal vessels are injected with Indian ink. ×19.

FIG. 25—Transverse section of the uterus of a pregnant sow in which the vessels have been injected with Indian ink to show the dense capillary plexus immediately under the epithelium. One of the radial arteries (A) supplying this plexus is also shown. ×15.

FIG. 26—Transverse section of the uterus of a pregnant sow in which the blood-vessels have been injected with Indian ink. The subepithelial plexus and its draining veins (V) are well shown. Note also the blood supply of the serous coat and of a gland (G.B.). ×7.

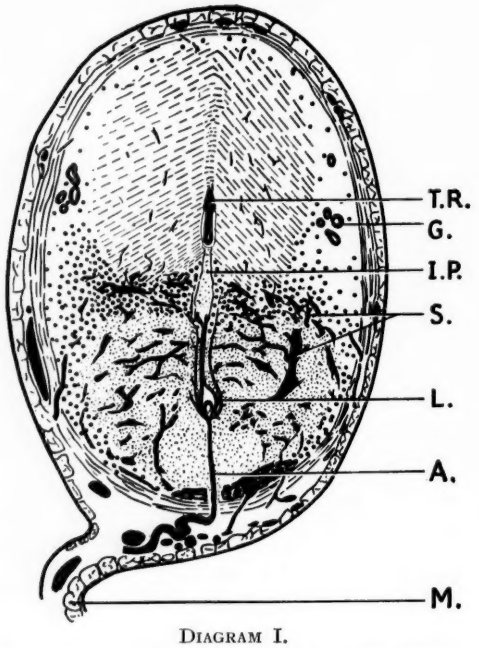

DIAGRAM I.

Diagram to illustrate the vascular arrangements in the uterus of the rat at the 8th day of pregnancy based on the serial sections of specimen R22. Note the malorientation of the embryo.

Decidua capsularis is hatched. Decidua basalis is stippled, the glycogenic zone being coarsely stippled and the central area of the myometrial region (Krehbiel) finely stippled.

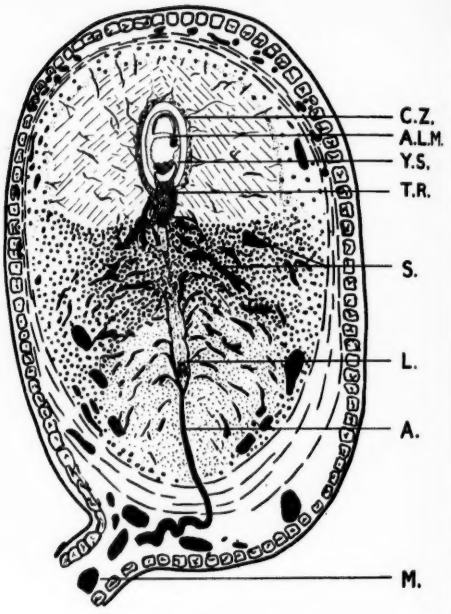

DIAGRAM II.

Diagram to illustrate the vascular arrangements and the decidual zones in the uterus of a rat at the 9th day of pregnancy.

Decidua capsularis, hatched; glycogenic zone coarsely stippled; central zone of mesometrial region (Krehbiel) finely stippled.

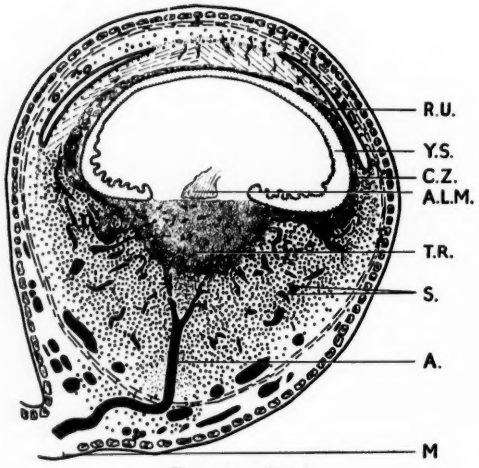

DIAGRAM III.

Diagram of the foetal membranes, decidual zones and vascular arrangements in the uterus of the rat on the 10th day of pregnancy.

Decidua capsularis hatched; glycogenic zone coarsely stippled; central zone of the mesometrial region (Krehbiel) finely stippled.

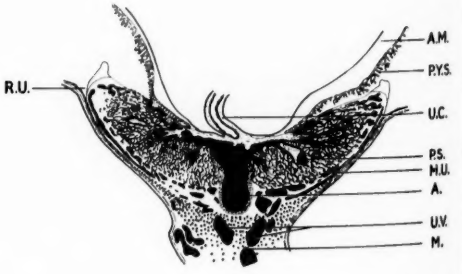

DIAGRAM IV.

Diagram of the foetal membranes and vascular arrangements in the placenta of the rat at the 18th day of pregnancy.

The myometrial gland is coarsely stippled.

oids of the basalis on the 8th and 9th days are indicative of a slow and sluggish circulation. Moreover, the degenerating "papilla" of stroma and epithelium, facing the mouth of the implantation pit on the 7th to 9th day in the rat, presents definite evidence for the arterial spasm. The arteries come from the mesometrium, through the circular muscle and very close to the underside of this papilla, before bifurcating and continuing into the superficial capillary plexus on either side of the implantation pit. This papilla represents the central point of the field supplied by the arteries. When they go into spasm it seems probable that the whole of the blood supply to the area of the papilla is cut off, with the result that it undergoes degeneration. The phenomena of oedema followed by epithelial and subepithelial sloughing of the endometrium during implantation is known in many species, including the primates, and is almost certainly consequent on vascular changes in the underlying tissues. Mossman (1937) discusses this.

In at least three species (rat, sheep, human) implantation is characterized by arterial spasm with capillary and venous dilatation and engorgement, giving the implanting embryo the opportunity of establishing its vascular relations with a static pool of blood at low pressure, thus reducing the risk of embryonic damage which might result from a blood stream flowing along under pressure. In the pig where there is no real implantation of foetal tissues within the uterine wall, the maternal blood-vessels remain continuously in this stage of post-arterial dilatation. Although Goldstein (1926) has indicated the importance of the glandular secretions and areolae in the nutrition of the pig embryo, both he and Amoroso (1947) have shown that the foetal blood stream penetrates the trophoblast and comes into very close relationship with the uterine tissues, so that the pig's placenta might be called epithelio-endothelial. These studies, together with those of Flexner and Gellhorn (1942), indicate that there is nevertheless a considerable transference of materials across the placenta directly from the one blood stream to the other. In the latter half of pregnancy, the arterial channels in the placenta become large and dilated, especially in the rat, but also in the sheep and cat. This almost certainly results in a fall of blood pressure and a reduction in the rate of flow in the wide, placental, arterial channels. The prolongation of the time taken by the maternal blood to circulate through the labyrinth allows a more complete exchange between the foetal and maternal blood streams. As regards the fall in blood pressure, it can only be assumed that the pressure must be approximately equal in the maternal and foetal blood streams within the labyrinth. Excessive pressure on the maternal side would presumably lead to collapse of the foetal capillaries. These facts may be relevant to some of the work of Huggett and Pritchard (1945) and Pritchard and Huggett (1947). They found that if the foetus was killed before the allantoic mesoderm had reached the placenta, the latter was killed by maternal haemorrhages, whereas after the invasion of the mesoderm into the placenta foetal death was not followed by placental death, but the foetal blood-vessels in the placenta were obliterated. According to Barcroft (1946), the umbilical arterial pressures continue to rise throughout most of pregnancy, whilst the venous pressures remain more or less fixed. Although the assumption that data obtained on the sheep will hold good for the rat is extremely uncertain, if the venous pressure in the rat's umbilical cord and placenta does not rise as gestation proceeds, it will be seen that the blood pressure in the maternal arterial channels, which are related most closely to the venous

end of the foetal capillaries in the labyrinth, must also remain at the same level throughout the latter half of pregnancy. Since this pressure must approximate to that of the foetus, some means of reducing the maternal arterial pressure must obtain, probably by the increased capacity of the maternal "arteries" in the placenta.

Finally, some comment may be made on the relationship between the "placental sign" in the rat and that in the macaque monkey. The "placental sign" consists of the presence of blood in the vagina, which may or may not be visible as an external flow. In the rat it extends from the 13th to the 16th days of gestation (Long and Evans, 1920) whereas in the macaque, it appears about the 17th day, and lasts for three weeks (Hartman, 1929). In the rat, the source of the blood of the "placental sign" is associated with the disintegration of the decidua capsularis and distal wall of the yolk-sac (Stafford, 1930); whereas in the monkey, Wislocki and Hartman (1929) have demonstrated in a 29-day pregnancy that the blood arises from the uterine glands, which are then engorged and greatly distended with blood. It will be quite obvious from this that the processes whereby the blood of the "placental sign" arises in the two animals are quite unrelated, both with regard to time of the bleeding in the gestation period and its source in relation to the embryo. In the rat, at any rate, it is a phenomenon more or less incidental to a very specialized degenerative process peculiar to rodents.

A search has been made for any process in the rat which, though it does not give rise to blood in the vagina, might in fact be comparable to the mechanism of the "placental sign" in the monkey. Such a phenomenon might be present on the 8th day of gestation, when the whole of the implantation pit is full of apparently fresh blood. This has extended out into the narrowed uterine lumen. Some of this blood is no doubt derived from the superficial sinusoids of the subepithelial plexus which have ruptured around the embryo; most of it seems to be concentrated in the part of the implantation pit away from the embryo, and to come from a more remote part of the plexus. Moreover, Krehbiel (1937) described an extravasation of blood on the 8th day, occurring in that elongated part of the pit between the embryo and the uterine lumen; this lifted the epithelium from its basement membrane and so initiated its degeneration. This phenomenon of passage of blood into the cavity of the uterus in a place a little removed from the direct action of the trophoblast may bear some correspondence to the "placental sign" of the macaque, but does not reach the vagina, because its passage down the uterus is hindered at the level of each implantation site by the extreme attenuation of the lumen there. The few glands which remain visible on the 8th day show no significant quantities of blood. None communicate with the implantation pit, where as in the macaque they are prominently distended by large volumes of blood and open into the uterine lumen. There is little resemblance between the bleeding in the macaque at such an early stage and the late "placental sign" of Long and Evans in the rat. The two phenomena are not analogous, whether the bleeding results from trophoblastic action or hormonal control. The 8th day extravasation into the implantation pit in the rat is more analogous to the early phenomenon in the monkey and also to that in the uterine glands of many early human implantations.

We are indebted to Professor H. A. Harris for his constant advice and encouragement. Our thanks are due to Mr. J. A. F. Fozzard for photography and

to Mrs. D. Davies and Mrs. E. J. Williams for help in the preparation of the manuscript.

References.

Amoroso, E. C. (1947): Communication to the Physiological Society at Cambridge, February.

Assheton, R. (1905): *Philos. Trans. roy. Soc. London, B*, **198**, 143.

Barcroft, J. (1946): *Researches on prenatal life*. Vol. I. Blackwell. Oxford.

Barcroft, J., and Barron, D. H. (1946): *Anat. Rec.*, **94**, 569.

Bremer, J. L. (1916): *Amer. J. Anat.*, **19**, 179.

Duval, M. (1891): *J. Anat., Paris*, **27**, 24, 344, 515.

Everett, J. W. (1935): *J. exp. Zool.*, **70**, 243.

Flexner, L. B., and Gellhorn, A. (1942): *Amer. J. Obstet. Gynec.*, **43**, 965.

Goldstein, S. R. (1926): *Anat. Rec.*, **34**, 25.

Grosser, O. (1909): *Vergleichende Anatomie und Entwicklungsgeschichte der Eihäute und der Placenta*. Braumüller. Wein and Leipzig.

Grosser, O. (1927): *Frühentwicklung, Eihautebildung und Placentation des Menschen und der Säugetiere*. Bergmann. München.

Hartman, C. G. (1929): *Bull. Johns Hopk. Hosp.*, **44**, 155.

Hill, J. P. (1932): *Philos. Trans. roy. Soc. London, B*, **221**, 45.

Huber, G. C. (1915): *J. Morphol.*, **26**, 247.

Huggett, A. St. G., and Pritchard, J. J. (1945): *Proc. R. Soc. Med.*, **38**, 261.

Jenkinson, J. W. (1902): *Tijdschr. ned. dierk. Ver.*, 2nd ser., **7**, 124.

Jenkinson, J. W. (1913): *Vertebrate embryology*. Clarendon Press. Oxford.

Krehbiel, R. H. (1937): *Physiol. Zoöl.*, **10**, 212.

Long, J. A., and Evans, H. M. (1920): *Anat. Rec.*, **18**, 249.

Long, J. A., and Evans, H. M. (1922): *Mem. Univ. Calif.*, **6**, 1.

Marshall, F. H. A. (1903): *Philos. Trans. roy. Soc. London, B*, **196**, 47.

Mossman, H. W. (1926): *Amer. J. Anat.*, **37**, 433.

Mossman, H. W. (1937): *Contr. Embryol. Carneg. Instn.*, **26**, 129.

Noer, R. (1946): *Anat. Rec.*, **96**, 383.

Pritchard, J. J. (1947): *J. Anat. Lond.*, **81**, 352.

Pritchard, J. J., and Huggett, A. St. G. (1947): *J. Anat. Lond.*, **81**, 212.

Ramsey, E. M. (1938): *Contr. Embryol. Carneg. Instn.*, **27**, 68.

Schlegel, J. U. (1946): *Acta Anat.*, **1**, 285.

Selye, H., and McKeown, T. (1935): *Proc. roy. Soc. Lond., B*, **119**, 1.

Stafford, E. S. (1930): *Anat. Rec.*, **47**, 43.

Tafani, A. (1887): *Arch. ital. Biol.*, **8**, 49.

Wislocki, G. B., and Hartman, C. G. (1929): *Bull. Johns. Hopk. Hosp.*, **44**, 165.

Wislocki, G. B., and Streeter, G. L. (1938): *Contr. Embryol. Carneg. Instn.*, **27**, 1.

THE VAGINAL BACTERIAL FLORA AND OVARIAN DYSFUNCTION

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INTRODUCTION.

THE important observation that a direct association exists between ovarian activity and the deposition of glycogen in the cells of the vaginal wall was made by Miura (1928). Other workers too, notably Cruickshank and Sharman (1934), and Rakoff, Feo, and Goldstein (1944), have confirmed this, so that it is now generally agreed that the biological conditions in the sexually mature vagina are governed by oestrogens which bring about the proliferation of the vaginal cells containing abundant glycogen. At the cyclical shedding of these cells and their autolysis the glycogen is liberated. If the vaginal bacillus described by Döderlein is present, it undoubtedly breaks down the available glycogen with acid production, for it has now been shown by several workers, notably Cruickshank (1934), that this bacillus breaks down glycogen "in vitro". Cruickshank has also suggested that it is probable that glycogen is also broken down in the absence of the vaginal bacillus through the agency of a diastatic ferment derived possibly from the vaginal cells. A mechanism like this would result in breakdown products of glycogen being available to other organisms, and thus acid could result from the breakdown of glycogen with or without the aid of the vaginal bacillus, but in whichever way the acidity is produced, it is directly proportional to the glycogen content, and, as the vaginal bacterial flora is largely determined by the degree of acidity in that canal, it can also be taken as dependent on ovarian activity. In the mature vagina, therefore, in a subject with normal ovarian function, the bacterial flora is composed of acidophilic and aciduric organisms determined by the acid reaction in the vagina. These two features fit into the usually accepted Grade I of "vaginal cleanliness".

In the investigation to be described the material was collected from a group of 39 married women attending the Fertility Clinic at the Birmingham and Midland Hospital for Women. The examinations made numbered 52, and these were made as far as possible at different times in the menstrual cycles of the individuals. The sole complaint of the majority was infertility. They had been referred from the Gynaecological Out-patient Department because they were free from organic pelvic disease; nearly all of them gave a history of menstrual cycles which were within the normal limits, and, in each case, sterility in the husband had been excluded. Actually the group was originally chosen as one likely to show normal bacterial flora; but as the work proceeded, it was found that many of the subjects gave abnormal findings, and later it appeared probable that many of them were individuals with some degree of ovarian dysfunction.

TECHNIQUE OF EXAMINATION.

In each case material was collected from the vagina with the patient in the lithotomy position, and with the aid of a Sims's speculum. The vagina was thoroughly swabbed. To find the pH a vaginal washing was done with doubly distilled water of pH 7.0, using a syringe with a long metal nozzle (intrauterine syringe). As far as possible the washing was restricted to the posterior vaginal wall so as to avoid any admixture of alkaline cervical mucus. The readings were taken with a new "British Drug Houses" capillator.

Approximately 60 per cent of the examinations were made at the premenstrual phase of the menstrual cycle, and the remaining 40 per cent during the pre-ovulation period. In each case material was examined in hanging drop preparations, particularly for the presence of *Trichomonas vaginalis* (Donné) and this parasite was found in one case. Two direct smears were also made, one of which was stained by Gram's method and the other by Ziehl-Neelsen's method for acid-alcohol-fast bacilli. Acid-fast bacilli were found in one case, and were identified as *Bacillus smegma*.

OBSERVATIONS.

Hydrogen Ion Concentration.

The pH values were distinctly less acid than the accepted normal in the majority of cases. The premenstrual examinations gave pH values of 4.4 to 7.8 with an average of 6.5. Those taken during the oestral period, however, showed similar figures, the range of values being from 5.7 to 7.7 with an average of 6.4. The figures for individual cases are recorded in the accompanying table.

Direct Smears.

The number of leucocytes present are recorded in Table I by signs as follows:

		Case distribution
None	–	9
Occasional	±	13
Few	+	18
Moderate number	++	9
Numerous	+++	3

There was no absolute correlation between the number of leucocytes, or pus cells, as the case may be, with the pH values as suggested in the much quoted three grades of "vaginal cleanliness"; and the number of squamous epithelial cells was also very variable.

One column in the table records the presence of vibrio-like organisms in smear preparations. No vibrios, however, were obtained by special cultural methods suited to the isolation of vibrios, and, in fact, arguments, which suggest that gram-negative curved forms of diphtheroid bacilli may simulate vibrios in vaginal smears, have been put forward by the author elsewhere.*

Cultural Findings.

The main bacteriological findings are set out in the table, and the degree of bacterial population, as computed by the number of organisms seen in the direct smears, together with the amount of growth obtained in cultures, is indicated by plus signs.

In addition the following organisms were obtained: 1 beta haemolytic streptococcus which gave a negative soluble haemolysin test, 1 obligate anaerobic streptococcus, 1 obligate anaerobic bacillus of the *Bacteroides fragilis* type and, from 10 cases, *Diplococcus crassus*, a commensal gram-negative coccus, the importance of which has been reported elsewhere.*

All strains of staphylococci were tested

* To be published in the *Journal of Hygiene*.

Table I.

Showing the Findings in 52 Examinations of 39 Cases.

CASE	MENSTRUAL CYCLE	pH	LEUCOCYTES	VAGINAL BACILLI	DIPHTHEROID BACILLI	STAPHYLOCOCCI	"VIBRIOS" (SMEARS)	ENTEROCOCCI	COLIFORM BACILLI
1	Pre.	—	+	—	++	+	—	+	—
2	Pre.	4·4	—	++	—	—	—	—	—
3	Pre.	5·6	±	+++	—	+	—	—	—
3	18th	5·8	—	+++	—	+	—	—	—
4	Pre.	5·8	—	—	++	+	++	—	+
4	15th	6·9	±	±	++	+	+++	—	+
5	Pre.	6·8	—	+	+	+	—	—	—
6	Pre.	6·9	—	—	+++	+	—	—	—
7	Pre.	5·6	+	—	+	+	+++	—	—
7	Pre.	6·6	+	—	++	+	+++	—	++
8	18th	7·0	+	—	++	+	—	—	+
9	14th	6·8	++	—	+++	+	—	—	+
10	21st	4·4	++	+++	—	—	—	—	—
11	14th	6·6	+	—	++	+	+++	—	+
12	1st Men.	7·0	±	+	+	+	—	—	+
13	Pre.	7·5	++	—	+	+	++	—	—
13	Pre.	7·3	±	—	+	+	++	—	—
13	7th	7·7	+	—	++	+	+++	+	—

TABLE I (*Continued*)

CASE	MENSTRUAL CYCLE	pH	LEUCOCYTES	VAGINAL BACILLI	DIPHTHEROID BACILLI	STAPHYLOCOCCI	"VIBRIOS" (SMEARS)	ENTEROCOCCI	COLIFORM BACILLI
14	Pre.	6·9	++	—	++	+	—	—	+
15	Pre.	6·9	+	—	+	+	++	—	—
16	Pre.	7·7	+	+++	++	—	—	—	—
17	16th	7·3	+++	—	++	+	+++	—	—
17	Pre.	—	++	—	+++	+	—	+	—
18	Pre.	6·8	+++	—	++	+	+++	—	—
19	Pre.	7·0	±	—	+++	+	—	+	—
19	12th	6·8	±	—	+++	+	+	+	—
19	Amen.	7·2	+	+	+	+	—	—	—
20	Pre.	4·6	±	++	+	+	—	—	+
21	Pre.	6·7	—	±	++	+	+++	+	—
22	Pre.	7·8	+	—	+++	+	—	—	—
22	8th	6·8	+	—	+++	+	—	—	—
23	Pre.	7·3	++	+	+++	+	+	—	—
23	Pre.	6·6	—	+	+++	—	+	—	—
24	Pre.	6·0	+	+	+++	+	++	—	—
24	14th	5·7	+	++	+	—	—	—	—
25	Pre.	7·8	++	—	+++	+	—	—	+

TABLE I (*Continued*)

CASE	MENSTRUAL CYCLE	pH	LEUCOCYTES	VAGINAL BACILLI	DIPHTHEROID BACILLI	STAPHYLOCOCCI	"VIBRIOS" (SMEARS)	ENTEROCOCCI	COLIFORM BACILLI
26	Pre.	6·9	±	++	+	+	—	—	—
27	Pre.	6·9	±	+++	+	+	—	—	—
28	Pre.	7·0	±	++	++	+	—	+	—
29	Pre.	4·6	+	+++	—	—	—	—	—
30	21st	7·8	+	±	++	+	—	—	—
31	Pre.	7·7	++	—	+++	—	—	—	—
32	Pre.	7·6	+	+++	+	+	—	—	—
33	10th	7·0	+++	±	+++	—	—	—	—
33	17th	5·8	++	+	+++	—	—	—	—
34	12th	6·6	±	—	+++	+	—	—	—
34	7th	6·9	—	—	—	+	—	—	+
35	16th	6·8	+	+	++	—	+	—	—
36	16th	7·0	+	—	++	—	+	—	+
37	Pre.	4·5	—	+++	—	—	—	—	—
38	15th	6·9	±	—	++	+	—	—	—
39	10th	5·7	+	++	—	—	—	+	—

for the production of plasma-coagulase with negative results.

Comment.

From the findings it is evident that 13 of the cases: Nos. 2, 3, 10, 16, 20, 24, 26, 27, 28, 29, 32, 37, and 39, will fit into Grade 1 of vaginal cleanliness, if one accepts as a criterion of Grade 1 an almost exclusive population of Döderlein's bacillus in the vagina independent of the pH value. The pH values of these cases, however, show a wide range of variation, from 4.4 to 7.7. According to the generally accepted standards of a Grade 1 classification, only Nos. 2, 10, 20, 29, and 37, in which cases the pH values vary from 4.4 to 4.6, are eligible for inclusion in Grade 1. All the others have a pH value of over 5.7. The number of leucocytes in this group varies from ++ to none.

Taking the absence of the vaginal bacillus, and the presence of other organisms such as coliform bacilli, enterococci, diphtheroid bacilli, and "vibrios" as criteria of a Grade 3 classification, 19 cases could be included in this grade, to wit, Nos. 1, 4, 6, 7, 8, 9, 11, 13, 14, 15, 17, 18, 19, 22, 25, 31, 34, 36, and 38. In these cases the range of pH values is from 5.6 to 7.8. The number of leucocytes in this group varies from +++ to none.

Seven cases remain, namely, Nos. 5, 12, 21, 23, 30, 33, and 35. These show only a small content of vaginal bacilli in a mixed flora associated with a pH range of 5.8 to 7.8, but this range is almost identical with that of the last-mentioned group. In fact, if considered on the pH range alone without reference to the presence or absence of the vaginal bacillus, these 7 cases could be allotted to Grade 3. The leucocytes in this group vary from +++ to none.

It is evident that in these findings there is no absolute correlation between the bacterial flora and the two accessory grading factors, namely the pH and the number of leucocytes, but that there is some overlapping. Considered on the pH values alone, 34 of the 39 cases could be allotted to Grade 3, and, with the fall of acidity, the bacterial flora shows a gradual transition from one composed mainly of the acidophilic vaginal bacillus to a mixed flora with few or no vaginal bacilli, but of organisms which are favoured by a less acid reaction.

The significance of the varying number of leucocytes is uncertain but, after a special study of vaginal diphtheroid bacilli, the author thinks that it is possible that some may act as low grade irritants under certain conditions.

Although the actual number of infertile women studied is relatively small, there appears to be ample evidence that, in the majority, the reaction of the vagina and the bacterial flora are abnormal by comparison with the accepted normal standards for sexually mature women. The author suggests that the deposition of vaginal glycogen is deranged and that the findings are indicative of ovarian dysfunction.

Summary.

An examination of a group of 39 women attending a fertility clinic has shown that the majority possessed abnormal vaginal pH values, and therefore showed a tendency to acquire abnormal bacterial flora. It is suggested on *a priori* grounds that these findings are indicative of ovarian dysfunction.

I wish to express thanks to Miss D. M. Shotton for access to clinical material.

References.

Cruickshank, R. (1934): *J. Path. Bact.*, **39**, 213.

Cruickshank, R., and Sharman, A. (1934): *J. Obstet. Gynaec.*, **41**, 190, 208.

Miura, H. (1928): *Mitt. med. Akad. Kioto.*, **2**, 1.

Rakoff, A. E., Feo, L. G., and Goldstein, L. (1944): *Amer. J. Obstet. Gynec.*, **47**, 467.

EXTERNAL VERSION UNDER ANAESTHESIA

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IN cases in which a breech presentation is discovered during pregnancy all the standard British textbooks of midwifery advise that prophylactic external version should be attempted, and most of these textbooks also recommend that in the cases in which version fails a further attempt should be made under anaesthesia. In spite of the almost unanimous advice of these teachers the authors were surprised to discover that in many hospitals external version under anaesthesia is not attempted, on the ground that it is highly dangerous to the foetus; and further, that it is considered impossible to perform version if the legs of the foetus are extended. When we referred to the literature we found that there were surprisingly few recorded series of cases of external version under anaesthesia. In fact, apart from cases listed without details in the clinical reports of various hospitals, the only series with more than 10 cases of version under anaesthesia are those of White and Flew (1933) with 92 cases, Wrigley (1934) with 76 cases, and Newell (1941) with 48 cases. Many authors recommend external version "with an anaesthetic if necessary", or in "exceptional cases", but do not specify the number of cases anaesthetized, and imply or state that they are few. In most of the reported series no distinction was made between primigravidae and multigravidae, and in none could we find any separation of cases with flexed or extended foetal legs. We therefore thought it might be of value to review our own cases, with the particular object of discovering the value or danger of external version under anaesthesia, and especially in cases in which the foetal legs were extended.

We have included all cases in which external version was attempted under anaesthesia, and in whom the result at delivery was known. During the war years external version was performed or attempted on a number of patients who were subsequently delivered in other hospitals and, though we have written to each patient, we have been unable to secure information of the result at delivery in some of these cases. Although the foetal heart was audible after version in all these, we have excluded them, as relevant stillbirths and recurrent breech presentations might otherwise have been omitted from our results (see Table I). Comparison of the cases in this table with those in later tables shows that the proportion of primigravidae and the proportion of successful versions was somewhat higher than for the series as a whole, so that this exclusion does not favourably bias our results.

We wish to emphasize that in all cases one or more unsuccessful attempts at version without anaesthesia had been made before an anaesthetic was given, and the cases we are reporting, therefore, represent

TABLE I.

Cases excluded because the result at delivery was unknown.

(In all cases the foetal heart remained audible for as long as the patients remained under observation.)

	No. of cases
Primigravidae:	
Version successful	34
Version successful, breech recurred, success repeated	1
Version failed, success at second attempt	1
Version failed, one attempt	3
Version failed, two attempts	1
	40
Multigravidae:	
Version successful	4

the more difficult cases. This is borne out by the observations that in 206 cases in which version was successful the breech presentation recurred in only 5, and that in 30 cases in which version failed subsequent spontaneous cephalic version occurred in only 1 case.

Technique of version. There has been nothing unusual in the technique of version that we have employed. As a routine we attempt version under anaesthesia between the 34th and 37th weeks in all cases in which version has failed without an anaesthetic. In cases in which a breech presentation is diagnosed at a later stage and version fails without an anaesthetic, we do not hesitate to attempt version under anaesthesia, and in 12 cases (6 in primigravidae) version was successful even at term. Apart from cases of twin pregnancy, and cases in which Caesarean section was proposed for some other reason, version has been attempted in nearly all cases diagnosed. In cases of doubtful disproportion version has sometimes been performed so that the relative size of the head and brim could be estimated.

The choice and depth of the anaesthetic is of the first importance, and the success of the operation greatly depends upon it. Unless really deep anaesthesia is used there is no advantage, and sometimes a positive disadvantage, in giving an anaesthetic. We have on different occasions tried a variety of anaesthetic agents, but for the great majority of cases have used gas, oxygen and ether, usually preceded by a full dose of morphia. The anaesthetic must be pushed to the level of deep surgical anaesthesia, when the abdominal wall is completely relaxed, and if morphia and ether are used we believe that the uterus is also relaxed. Chloroform is equally effective, but we have not used it on account of its greater danger. Other agents have proved ineffective in securing full relaxation with safety. We have lately tried curare, and though complete relaxation of the abdominal wall is obtained, we consider that the uterine tone is increased with this drug, and do not recommend it. There have been no accidents or significant complications due to the anaesthetics used in these cases.

As a routine, morphia (gr. $\frac{1}{3}$ or $\frac{1}{4}$) and atropine are given 1 hour beforehand, at which time the patient is placed in the Trendelenburg position. After ensuring that the bladder is empty, deep anaesthesia is induced. The breech is first disengaged from the pelvis. In a very few exceptional cases we have applied pressure through the posterior vaginal fornix to achieve this, but if the breech cannot be disengaged by abdominal manipulation it is doubtful wisdom to persist with attempts at vaginal pressure. The head is then pushed in the direction of flexion, that is the direction in which the foetus faces. This can be most difficult if the head is tucked under the costal margin, and it is

sometimes best to push the head to one side and somewhat down before pushing the breech up. If version is difficult in the usual direction of flexion it is attempted in the opposite direction, and this is often the most profitable direction if the foetal legs are extended, as the movement of the foetus may flex the legs and thereby make the version easier. There is undeniably a certain knack in version, and practice begets success. Frenzied violence or jerky movements are never employed, though considerable pressure with the fingers can safely be used. Immediately after version the foetal head may remain high, due to extension of the head, or in some cases to persistent extension of the legs. Quite often, however, the head sinks down into the pelvis with surprising ease and rapidity. In cases in which the head remains high an attempt is made to assess the fit of the foetal head to the brim, but often this is not possible until a day or two later, when the foetus has settled into its new position. There is, therefore, no need to be concerned over a high head immediately following version. A binder and lateral pads are usually applied for so long as the patient remains in bed, commonly the day following.

Results. The following tables set out our results. It will be seen from Table II that in primigravidae, version was ultimately successful in 149 out of 172 patients (87 per cent), in whom 152 out of 185 attempts at version were successful (82 per cent). In multigravidae version was ultimately successful in 57 out of 64 patients (89 per cent), in whom 59 out of 68 attempts at version were successful (87 per cent).

If the only cases considered are those in which the foetal legs were proven to be extended by X-rays or at delivery, then the following results are obtained (Table III). In primigravidae, version was ultimately successful in 65 out of 82 cases (79 per cent), and in these cases 65 out of 91 attempts at version were successful (71 per cent). In multigravidae, version was ultimately successful in 23 out of 30 cases (77 per cent), and in these cases 24 out of 33 attempts at version were successful (73 per cent). It is probable that the legs were in fact extended in the majority of the other cases, bearing in mind the fact that previous version without anaesthesia had been unsuccessful. During the years 1946 and 1947 every such patient was X-rayed as a routine, and in 82 per cent of the total requiring version under anaesthesia the legs were shown to be extended, and there is no reason to suppose that the incidence was different in the other years.

Foetal mortality. The methods of ultimate delivery of these women are set out in Table II, together with all cases of foetal death. From the table it will be seen that among 172 cases of version under anaesthesia in primigravidae 10 foetal deaths occurred. However, 6 of these were clearly unrelated to the version: gross congenital anomalies in 3 cases, tentorial tears in the subsequent labour in 2 cases, and 1 case in which the foetal heart was audible for 6 weeks after version and during 48 hours of a long first stage of labour. Among 64 cases of version under anaesthesia in multigravidae 4 foetal deaths occurred, but none of these were attributable to the version, being due to haemolytic disease in 1 case, tentorial tear in subsequent labour in 1 case asphyxia during breech delivery in 1 case, and in the fourth case the foetal heart was heard for several weeks after version, and no abnormality of the placenta or cord was found at birth. Among these 236 cases of version under anaesthesia 2 foetal deaths were certainly due to version; a case of prolapse of the cord, and a case of difficult labour due to a compound presen-

TABLE II.

Cases of External Version under Anaesthesia in which the result at delivery is known.

PRIMIGRAVIDAE. 172 cases (185 attempts at version).

Result of version		Method of delivery of these cases		Foetal deaths	Foetal deaths attributed to version
Successful	140	Normal delivery	114	2 spina bifida 1 osteogenesis imperfecta 1 prolapsed cord	1 prolapsed cord
Successful, but breech recurred. Success repeated	3				
Failed, but success at second attempt	6	Forceps delivery	26	1 tentorial tear 1 foetal heart heard until labour 6 weeks later. Died after long first stage.	
Total	149	Caesarean section (disproportion 4, placenta praevia 1)	8		
		Internal version and breech extraction for compound presentation	1	1 compound presentation	1 compound presentation
		Normal delivery	1		
Failed, spontaneous version	1	Breech delivery	17	1 tentorial tear 1 macerated 1 cause unknown	1 macerated 1 cause unknown
Failed, one attempt	18				
Failed, two attempts	4				
Total	23	Caesarean section	5		
Sum Total	172	Totals	172	10	4

MULTIGRAVIDAE. 64 cases (68 attempts at version).

Successful	54	Normal delivery	55	1 haemolytic disease 1 foetal heart heard until labour. No abnormality of placenta or cord	
Successful, but breech recurred, success repeated	2				
Failed, but success at second attempt	1	Caesarean section	2		
Total	57				
Failed, one attempt	6	Breech delivery	6	1 tentorial tear 1 asphyxia during breech delivery	
Failed, two attempts	1				
Total	7	Caesarean section	1		
Sum Total	64	Totals	64	4	0

GRAND TOTALS: 236 cases (253 attempts at version).
4 foetal deaths attributed to version (1.7 per cent).

TABLE III.

Cases of External Version under Anaesthesia in which the result at delivery is known, and the foetal legs were seen to be extended in an X-ray or at delivery.

PRIMIGRAVIDAE. 82 cases (91 attempts at version).

Result of version		Method of delivery of these cases		Foetal deaths	Foetal deaths attributed to version
Successful	60	Normal delivery	47		
Failed, but success at second attempt	5	Forceps delivery	14	1 tentorial tear 1 foetal heart heard until labour 6 weeks later. Died after long first stage	
Total	65				
		Caesarean section	3		
		Internal version and breech extraction for compound presentation	1	1 compound presentation	1 compound presentation
Failed, spontaneous version	1	Normal delivery	1		
Failed, one attempt	12	Breech delivery	12	1 tentorial tear	
Failed, two attempts	4	Caesarean section	4		
Total	17				
Sum Total	82	Totals	82	4	1

MULTIGRAVIDAE. 30 cases (33 attempts at version).

Successful	21	Normal delivery	22	1 haemolytic disease 1 foetal heart heard until labour. No abnormality of placenta or cord	
Successful, but breech recurred. Success repeated	1				
Failed, success at second attempt	1	Caesarean section	1		
Total	23				
Failed, one attempt	6	Breech delivery	6	1 tentorial tear 1 asphyxia during breech delivery	
Failed, two attempts	1				
Total	7	Caesarean section	1		
Sum Total	30	Totals	30	4	0

GRAND TOTAL: 112 cases (124 attempts at version).
1 foetal death attributed to version (0.9 per cent).

tation, feet and head. In 2 other cases the cause of death was uncertain but may have been due to the version. The foetal mortality due to external version under anaesthesia may, therefore, be stated as 4 in 236, or 1.7 per cent. If we consider only the cases in which the legs were proven to be extended (Table III) there was 1 foetal death, that due to a compound presentation, among 112 cases, so that the risk is not shown to be greater for these cases.

Complications. Among these 236 cases (253 attempts at version) premature onset of labour occurred in 7 cases, but without stillbirth or neonatal death. The cord prolapsed in 1 case, and the foetus was stillborn. In 1 case of compound presentation the foetus was stillborn, but in another case of prolapse of the arm the child was born alive. Vaginal bleeding was recorded in only 5 cases, but slight bleeding certainly occurred in a larger number of cases. There were no stillbirths among these cases of vaginal bleeding.

Success-rate at different weeks. Table IV sets out the success-rate when version was attempted at different weeks of pregnancy. When dates were uncertain, cases were omitted from this table.

Discussion.

Many who allow the value of external version without anaesthesia maintain that an anaesthetic increases the foetal risk, especially Wrigley (1934), who utterly condemns the use of an anaestetic, Gibberd (1927), White and Flew (1933), Danforth and Galloway (1938), Taussig (1931), Dieckmann (1946), and Mengert (1947). The risks mentioned are placental separation, sometimes with external bleeding, premature separation of the membranes, the premature onset of labour, prolapse of the cord, or the prolapse of a limb beside the presenting part. It is not denied that all these accidents may occasionally occur, but in the present series they have been infrequent, as stated above.

Although none of the reported series separate the cases with extended foetal legs, several authors state that version is either impossible or dangerous if the legs are extended. Siegel and McNally (1939) do not attempt version if an X-ray reveals an extended breech. Randall (1934) abandons version if the breech cannot easily be disengaged. Donovan (1932) states that it is usually impossible to turn

Table IV.

To show success rate of version under anaesthesia at various weeks of pregnancy.

	All cases			Cases with extended legs		
Primigravidae	Success	(per cent)	Failure	Success	(per cent)	Failure
32–33 weeks	12	100	0	6	100	0
34–35 ,, ...	58	86	9	22	73	8
36–37 ,, ...	47	75	16	24	59	17
38–39 ,, ...	22	73	8	6		5
40–42 ,, ...	7		1	3		0
Multigravidae						
34–35 weeks	17	89	2	8	80	2
36–37 ,, ...	25	93	2	13	87	2
38–39 ,, ...	10	77	3	2		3
40–42 ,, ...	7		0	1		0

246 attempts. 7 cases omitted as dates uncertain.

TABLE V.

To show reported mortality of uncomplicated breech delivery.

Author	Cases excluded	Total No. of cases	Primi-gravidae	Foetal mortality per cent	Multi-gravidae	Foetal mortality per cent
King and Gladden (1929)	Infants under 5 pounds, macerated infants, twins.	158	78	7.7	80	12.5
McGuinness (1928)	Complicated cases, premature and macerated infants, congenital abnormalities.	86	30	13.3	56	23.2
Irving and Goethals (1926)	Complicated cases, twins, premature and macerated infants, congenital abnormalities.	235	94	12.7	141	7.8
Gibberd (1931)	Complicated cases, twins, macerated infants.	209	48	29.0	161	17.0
Macafee and McClure (1937)	Complicated cases.	246	100	10.0	146	3.4
Roy (1936)	Complicated cases, twins, premature and macerated infants, congenital abnormalities.	155	77	10.3	78	8.9
Patton and Mussey (1940)	Premature and macerated infants, congenital abnormalities.	261	131	5.3	130	2.2
Taussig (1931)	Premature and macerated infants.	162	83	12.0	79	9.0
Queen Charlotte's Hospital Reports (1939–45)	Complicated cases, twins, premature and macerated infants, congenital abnormalities.	145	97	13.4	48	12.5
Totals		1657	738	11.3	919	9.8

a frank breech if the legs are closely together. Dearnley (1931) writes "if the legs are extended fully and there is also extension of the child's body it is wiser not to do version, as when this is performed with force under anaesthesia damage may be done, and there is also risk of bringing a hand or arm down by the side of the head, which will cause difficulty in labour." In America even more extreme views are frequently expressed. For example Stein (1941) condemns external version altogether in cases of extended breech presentation as failure is stated to be common, and attempts at version may increase attitudes of deflexion. Another common American opinion is represented by Henderson (1941), who condemns external version, as he considers that a flexed breech is easy to deliver, while with an extended breech external version is dangerous and commonly fails.

Wrigley's paper (1934) deserves special mention, both because he has collected 76 cases of version under anaesthesia from hospital reports, and also because of his violent condemnation of the operation. Among these 76 cases he found 45 cases of successful version, but among these 10 stillbirths occurred (13 per cent), which result he contrasts with a mortality of 10 per cent for breech delivery. The causes of these stillbirths are not set out in detail and may not, in fact, have been due to the versions; in any case our results are very different, both as regards mortality and the success of version.

Obviously, external version under anaesthesia can be justified only if the risk of the operation, bearing in mind the success-rate, is less than the risk of vaginal breech delivery. The foetal mortality in breech deliveries has been much studied, and many large series of breech deliveries have been published. It would appear to be a simple matter to compare and correlate these published figures, but unfortunately the different authors are inconsistent in their methods of recording their results. Some reports do not separate primigravidae and multigravidae; some do not distinguish cases in which there was some other obstetric complication such as placenta praevia or disproportion: and conversely some authors even regard extended legs as a complication. Some

TABLE VI.
Reported results of version without anaesthesia.

Author	All cases		Primigravidae		Multigravidae		No. of cases with anaesthesia
	No. of cases	Successful	No. of cases	Successful	No. of cases	Successful	
Gibberd (1927)	232	204	—	—	—	—	9
Newell (1941)	775	709	234	191	541	518	48
Trubkowitch and Archangelsky (1944)	247	228	—	—	—	—	4
Ryder (1943)	214	198	—	—	—	—	—
Donovan (1932)	91	80	47	38	44	42	—
Bartholomew (1927)	54	39	26	15	28	24	2
McGuinness (1928)	59	57	24	23	35	34	2
Thornhill (1936)	58	49	23	18	35	31	2
Siegel and McNally (1939)	68	55	21	15	47	40	—
Glassman (1932)	64	61	10	9	54	52	—
Totals	1862	1680	385	309	784	741	—
Percentages		90		80		94	—

In some of these cases more than one attempt at version was made before final success.

series include deaths due to prematurity, malformations, and deaths before labour. The following authors plainly state their criteria for "uncomplicated" breech delivery, and separate primigravidae and multigravidae, and it will be seen that there is more agreement between them than is usual in the larger series commonly quoted (Table V).

From these figures it may reasonably be assumed that the foetal mortality for mature uncomplicated breech delivery is about 11 per cent in primigravidae, and slightly less in multigravidae, and this is the figure with which the results of external version must be compared.

We have reported successful version under anaesthesia in 87 per cent of primigravidae, and in 89 per cent of multigravidae, but we repeat that in all these cases version had previously failed without an anaesthetic. These are the more difficult cases, and the "success-rate" must be much higher if all cases of antenatal version are included. Many authors have reported their results in version without anaesthesia (Table VI).

As regards the foetal mortality due to version without anaesthesia the following figures are available:

	Total No. of cases	No. of cases anaesthetized	Foetal deaths
Siegel and McNally (1939)	68	0	1
Thornhill (1936)	58	2	0
Bartholomew (1927)	54	9	0
Gibberd (1927)	232	9	2
McGuinness (1928)	59	2	1
Macafee and McClure (1937)	134	0	0
Ryder (1943)	214	0	0
Trubkovitch and Archangelsky (1944)	247	4	3
Newell (1941)	785	48	24
Total	1851	—	32
Percentage			1.7

As regards cases in which an anaesthetic was given for version, very little data is available. From Queen Charlotte's Hospital Reports (1938–45) the following figures can be derived: Primigravidae 197 cases, of which 144 were successful; multigravidae, 51 cases, of which 37 were successful. Newell (1941) reported only 18 successes in 48 cases, but it may be remarked that 36 of these cases were given pentothal, a most unsuitable anaesthetic. It is not possible to discover the foetal mortality from the published figures, except that Wrigley (1934) reported 10 stillbirths following version in 45 cases, but as already remarked he gives no details of the causes of these deaths, which may have been quite unconnected with the versions.

We consider that our results are fairly representative and could easily be equalled or bettered by others. If the foetal risk from version is 1.7 per cent, and the probability of success under anaesthesia over 85 per cent, even in cases in which version has previously failed without an anaesthetic, the operation is clearly justified. We can perhaps illustrate our opinion thus: if 1,000 cases are treated by version there will be about 17 foetal deaths due to the operation, and about 15 foetal deaths in cases in which version fails and breech delivery occurs. On the other hand, if all the cases were delivered as breech presentations, there would be about 100 foetal deaths due to breech delivery alone. We therefore urge the more general adoption of external version under deep anaesthesia in the cases in which version has otherwise failed, and maintain that the operation is not unduly dangerous, and that it is possible even in cases in which the foetal legs are extended.

Summary.

The results of external version under anaesthesia in 236 cases of breech presentation in which version had previously failed

without anaesthesia are reported. Version was successful in 206 of these cases, and the foetal mortality due to version under anaesthesia in these cases was 1.7 per cent. The results and technique are presented in detail.

REFERENCES.

Bartholomew, R. A. (1927): *Amer. J. Obstet. Gynec.*, **14**, 648.

Danforth, W. C., and Galloway, C. E. (1938): *Amer. J. Obstet. Gynec.*, **35**, 123.

Dearnley, G. (1931): *Brit. med. J.*, **2**, 371.

Dieckmann, W. J. (1946): *Amer. J. Obstet. Gynec.*, **52**, 349.

Donovan, H. C. E. (1932): *Med. J. Austral.*, **2**, 617.

Gibberd, G. F. (1927): *J. Obstet. Gynaec.*, **34**, 256.

Gibberd, G. F. (1931): *Brit. med. J.*, **2**, 369.

Glassman, O. (1932): *Amer. J. Obstet. Gynec.*, **24**, 277.

Henderson, H. (1941): *Discussion of paper of Stein, I. F.* (below).

Irving, F. C., and Goethals, T. R. (1926): *Amer. J. Obstet. Gynec.*, **11**, 80.

King, E. L., and Gladden, A. H. (1929): *Amer. J. Obstet. Gynec.*, **17**, 78.

Macafee, C. H. G., and McClure, H. I. (1937): *Brit. med. J.*, **2**, 1112.

McGuinness, F. G. (1928): *Canad. med. assoc. J.*, **18**, 289.

Mengert, W. F. (1947): *Postgraduate Obstetrics*, Hamilton, London. p. 238.

Newell, J. L. (1941): *Amer. J. Obstet. Gynec.*, **42**, 256.

Patton, G. D., and Mussey, R. D. (1940): *Proc. Staff M. Mayo Clin.*, **15**, 389.

Randall, M. M. (1934): *Proc. Staff M. Mayo Clin.* **9**, 5.

Roy, D. (1936): *Proc. Roy. Soc. Med.*, **29**, 205.

Ryder, G. H. (1943): *Amer. J. Obstet. Gynec.*, **45**, 1004.

Siegel, I. A., and McNally, H. B. (1939): *Amer. J. Obstet. Gynec.*, **37**, 86.

Stein, I. F. (1941): *J. Amer. Med. Assoc.*, **117**, 1430.

Taussig, F. J. (1931): *Amer. J. Obstet. Gynec.*, **22**, 304.

Thornhill, P. E. (1936): *Virginia Med. Monthly*, **63**, 153.

Trubkowitch, M. V., and Archangelsky, B. A. (1944): *Brit. med. J.*, **1**, 220.

White, N., and Flew, J. D. (1933): *Brit. med. J.*, **2**, 346.

Wrigley, A. J. (1934): *Brit. med. J.*, **1**, 891.

CHILD-BEARING IN THE TUBERCULOUS GRAVIDAE

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INTRODUCTION.

MANY complex factors combine to render the investigation of the co-existing conditions of pregnancy and pulmonary tuberculosis a problem of considerable magnitude. Consequently, while its study to date has involved much labour and research, observations and conclusions are neither complete nor final.

So long as the basic principles of the entire cycle of pregnancy are imperfectly understood, and fundamental knowledge of the natural history of tuberculosis is lacking, finite assessment of this problem must be deferred.

The writers, in an attempt to clarify their own views on the correlation of child-bearing and pulmonary tuberculosis, carried out this present investigation, and the results of their personal observations on 150 consecutive tuberculous gravidae are recorded in this study.

RESULTS OF INVESTIGATION.

During the period, January 1947 to March 1948 inclusive, 150 pregnant, tuberculous patients were delivered in the maternity unit, Robroyston Hospital, Glasgow.

No selection was made in the patients admitted: all were recommended for admission from tuberculosis dispensaries and antenatal clinics, and accordingly results obtained may be regarded as applying to all types of tuberculous lung lesions associated with pregnancy.

Deterioration observed, clinically and radiologically during pregnancy, labour, and for approximately 2 to 3 months following delivery, was attributed to the effects of childbearing on the lung condition. Classification of tuberculous lung lesions being variable, it was decided for practicable purposes, to group patients on admission according to the following scale of assessments:

(1) "Quiescent" cases, in which the general condition of the patient was good; toxaemia was absent; tubercle bacilli were not present in the sputum, and serial skiagrams showed no sign of pulmonary progression.

(2) "Arrested" cases, in which the disease had been quiescent over a continuous period of 2 years.

(3) "Recovered" cases, in which the state of quiescence continued uninterruptedly for 5 years.

(4) "Active" cases, discharging tubercle bacilli in the sputum during the preceding 3 months.

Reference to Table I illustrates this grouping.

Of the total of 150 patients under review, 79 were primiparae, 71 multiparae, and

their ages varied from 19 to 38 years, with the exception of 2 who were over the age of 40.

TABLE I.

Type of disease	Number of cases
Quiescent	73
Arrested	13
Recovered	6
Active	58
Total	150

Table II is an attempt to correlate age and parity distribution with the clinical status of the patient at the end of the period of observation.

artificial pneumothorax induced, with section of adhesions in 7; one patient, 3½ months pregnant on admission, was the subject of a two-stage thoracoplasty operation.

One other patient was admitted with massive left-sided pleural effusion, for which paracentesis was necessary.

Tuberculosis ante-dated the pregnancy in 108 patients, in 11 of whom the operation of thoracoplasty had been carried out prior to admission, while in 10 others, artificial pneumothorax was maintained concurrently with the pregnancy. The remaining 87 patients gave a history of routine sanatorium treatment, with artificial pneumo-

TABLE II.

Age group (years)	Primiparae				Multiparae				Total
	Imp.	ISQ	Worse	Dead	Imp.	ISQ.	Worse	Dead	
19–23	6	16	1	2	2	5	3	0	35
24–28	5	25	4	3	4	17	4	3	65
29–33	2	8	0	2	5	11	2	4	34
34–38	0	4	0	1	1	7	0	1	14
Over 39	0	0	0	0	1	1	0	0	2
								Total	150

The following facts are elicited from the above Table: 30, or approximately 20 per cent of the total retrogressed, 13 or 43 per cent being primiparae, 17 or 50 per cent multiparae.

Scrutiny of case records showed that in 42 instances, or 28 per cent of the total, the pulmonary condition was discovered for the first time during pregnancy, and of this group, 4 cases were quiescent, 38 were active. Of the latter, 17 with advanced chest conditions retrogressed. Two of these were diagnosed early in pregnancy, 12 late; in the remaining 3 patients, all of whom died, diagnosis was made for the first time in the puerperium.

Collapso-therapeutic measures in their many forms were applied with success to 20 other patients during gestation: 12 had thorax in 53, and phrenic nerve interruption in 10. Four deaths were recorded in this group of patients.

With regard to the influence of the tuberculous lesion on the pregnancy, it was found that toxaemias were uncommon. High blood-pressure occurred in 3 cases, eclampsia in 1, and antepartum haemorrhage in 1.

Labours were little affected; their duration varied from 1 hour to 24 hours 15 minutes, with an average of 14 hours for the primiparae, and from one hour 20 minutes, to 26 hours 35 minutes, with an average of 9 hours for multiparae.

Dyspnoea of moderate degree was noticed in 18 patients during the height of the second stage of labour, and of these 2 had received thoracoplasty operations and

8 artificial pneumothorax treatment, while the remaining 8 patients suffered from advanced pulmonary tuberculosis. With the exception of 2 instances in which the afterbirth was manually removed, the placenta was expelled complete and spontaneous within 15 to 30 minutes. No spontaneous abortions occurred in the patients under discussion.

Portpartum haemorrhage occurred in 3 patients, puerperal sepsis in 1.

Reference to Table III illustrates the type of delivery and number of patients who went to term.

TABLE III.

Delivery	Primiparae	Multiparae	Total
Spontaneous ...	44	58	102
Spontaneous and episiotomy ...	8	2	10
Forceps	4	2	6
Forceps and episiotomy ...	14	2	16
		Total	134

Two multiparae, seen for the first time at the 6th month approximately, died undelivered; in both the lung lesion was advanced and bilateral, and in 1, tuberculous meningitis complicated the condition.

No deaths occurred during labour.

Table IV shows the number of patients on whom therapeutic interruption of the pregnancy was performed; clinical status at the end of the observation period is noted.

One hundred and thirty-seven infants were born to 132 patients, 119 or 86.5 per cent being normal, full-term, with death occurring in 3 cases. In addition, 1 infant, also delivered at term but with multiple congenital deformities, died soon after birth. Fourteen deaths occurred in 17 premature infants born.

Included in the group of premature deliveries were 5 sets of twins.

DISCUSSION.

Although some success has been met with, attempts made to solve the recurring problem of the tuberculous gravidae have been retarded by many adverse factors, not the least of which is the present-day regrettable ignorance of the basic pattern of the combined conditions. Recently, however, numerous careful and painstaking contributions have appeared, resulting in the revision of opinion on their reciprocal relationships.

Accordingly, in the management of the pregnant tuberculous patient, a principle of conservatism is now advocated, and this precept has been put into practice in the patients under review. Furthermore, in an endeavour by the local authorities, City of Glasgow, to bring the management of these patients under unified control, the effects of a conservative and unitarian approach to the problem have been observed. At this juncture, before undertaking discussion of

TABLE IV.

Method of termination	Primiparae					Multiparae				
	Imp.	ISQ.	Worse	Dead	Total	Imp.	ISQ.	Worse	Dead	Total
Surgical induction	0	0	0	0	0	0	0	0	1	1
D. & C.	0	0	0	0	0	0	0	0	1	1
Hysterotomy and sterilization ...	1	0	3	2	6	1	0	1	0	2
Hysterotomy without sterilization	1	1	1	0	3	0	0	0	0	0
Caesarean section	0	0	0	0	0	0	1	0	0	1
Total ...	2	1	4	2	9	1	1	1	2	5

the results, mention of their management must be made.

In February 1947 special provision was made in the maternity unit and associated antenatal and postnatal clinics, Robroyston Hospital, Glasgow, for the observation and treatment of expectant and nursing tuberculous mothers, all of whom, resident within the city, were eligible for admission. In order that contingencies of an obstetrical and medical nature might be investigated and treated simultaneously, the staff included a consultant obstetrician and a chest physician, while the responsibility for the infant after delivery and during the neonatal period devolved upon the paediatrician to the hospital. Breast feeding, except in certain selected cases, was forbidden.

In the patients under review prior consideration was given to the lung lesion, the pregnancy being regarded as secondary in significance. Where indicated, surgical procedures designed to secure partial and complete immobilization of the diseased lung were applied, not only during pregnancy however long its duration, but throughout the puerperium.

Decision to apply such measures was influenced by many factors, of which the following are noteworthy:

(1) Family history, (2) Previous sanatorium treatment, (3) Character and extent of the lung lesion, (4) Obstetrical history, past and present, with special reference to the reaction of the patient to her pregnancies.

Finally, consideration was given to factors common to both conditions, such as the age of the patient, socio-economic circumstances, and individual nutritional states.

Since surgical measures do not negative the need for rest, emphasis was laid on this important principle of tuberculosis therapeutics. Diet was supplemented by adequate amounts of calcium, iron and vitamins, in an attempt to bring about an optimum nutritional state, with its resulting high level of resistance.

When obstetrical problems were encountered they were dealt with in an orthodox manner. Where pregnancy was advanced less than 5 months, therapeutic interruption was performed if the case was one of advanced pulmonary tuberculosis in which collapse therapy was contra-indicated. Later than this period pregnancy was allowed to proceed to term and, where possible, labour was shortened and dystocia avoided. Spinal anaesthesia was preferred to inhalent drugs. On discharge from hospital advice was given the mother regarding contraception, and she was advised to report, with her child, to the postnatal clinic in 3 months' time for further assessment.

Conditions such as pregnancy and pulmonary tuberculosis with their diverse symptomatology and course, singly and collectively, make difficult the compilation of statistics of results, and the fallacy of formulating definite opinions on evidence presented in this study is obvious.

Table I shows that 50 per cent and 30 per cent of the total number of patients were quiescent and active respectively; the remainder were arrested and recovered cases.

Morbidity and mortality rates reached their peak in the present series (Table II) in age groups 24 to 28 years, affecting 37 primiparae and 28 multiparae, 14 or 21 per cent of which group of 65 patients deteriorated. In this group, pulmonary progression was the same for both primiparous and multiparous patients.

By comparison the incidence in age group 20 to 33 years, was 12 for the primiparae as against 22 for the multiparae; 2 or 16 per cent of the former, 6 or 27 per cent of the latter, deteriorated.

It is noteworthy that out of a total of 30 patients who showed evidence of progression of disease, 13 or 43 per cent were primiparae, 17 or 50 per cent multiparae. The numbers who showed improvement were approximately the same, 13 or 16 per cent for primiparae, and 13 or 18 per cent for multiparous patients.

While these figures are statistically insignificant to justify final pronouncements on the precise influence of age and parity on the evolution of pulmonary tuberculosis, the impression was formed that, generally, primiparae fared better than multiparae, presumably because the health of the latter had become impaired by repeated pregnancies and domestic responsibilities, resulting in lowering of the powers of resistance to a dangerous level. It is interesting to note that while Jameson (1935) supports this view, Cohen (1946) disagrees.

Of 42 patients in whom demonstrable lung lesions were discovered for the first time during pregnancy, 12 were diagnosed late in its course, death occurring in 7 cases, while 3 patients diagnosed tuberculous in the puerperium all died. In these 10 patients collapse therapy was contra-indicated on account of the nature and extent of the associated lung lesion. By contrast, 20 patients whose lesions were diagnosed early in pregnancy received this treatment, and it is significant that none revealed deterioration in the period under observation. The obvious conclusion, therefore, is that the later in pregnancy the diagnosis of tuberculosis is delayed the worse the prognosis.

Pregnant patients tolerate collapse therapy well, even thoracoplasty in certain selected cases (McIntyre, 1948), and pregnancy should not be regarded as a contra-indication to active forms of treatment.

Of 108 patients, the pulmonary lesion ante-dated pregnancy and, in the majority of cases, routine sanatorium treatment had been received: of this number only 4 patients died during the period of observation. This low mortality rate must be attributed to the fact that patients with known tuberculosis who become pregnant, and, at an early stage are brought under the surveillance of chest physicians, receive prompt and appropriate medical treatment. Experience teaches such patients not only the personal dangers of the disease, but also the hazards of contact infection, and concern for their child's welfare, no less than their own, leads them to seek advice early in pregnancy.

Of 134 patients who went to term, 70 were primiparae, 64 multiparae. Spontaneous delivery occurred in 122 patients, with episiotomy in 10, of whom 8 were primiparae.

Forceps were applied in 22 patients, with episiotomy in 16, 14 of the latter group being primiparae.

Postpartum haemorrhage was recorded in 3 instances, which is a small proportion of the total, and more favourable than the figure of 13 per cent given by Matthews and Bryant (1930) as the average incidence among parturient tuberculous patients.

Puerperal sepsis occurred in only 1 case, the condition being complicated by phlegmasia alba dolens.

The effect of the pulmonary lesion on the infants was almost negligible, 86.5 per cent being normal at birth, and in good general condition at the time of discharge from hospital; this figure corresponds very closely with that given by Barnes and Barnes (1930).

Five sets of twins were delivered.

Premature labours occurred in 17 patients, or 12.4 per cent of the total, in contrast to 8 per cent, which is the figure given as an average for the hospital generally. Since 14 of these patients suffered from advanced disease, the inference was that premature labour bore

a direct relationship to the lung lesion. The remaining 3 patients were delivered of twins. It is possible that in this latter instance plural pregnancy was the contributing factor.

As one would expect, the mortality rate was high among the premature infants. Autopsies failed to reveal evidence of existing congenital tuberculosis.

Premature evacuation of the uterus was carried out in 14 patients, 9 of whom showed subsequent deterioration, 6 of these being primiparae, 3 multiparae. While ceding the point that pregnancy may have an adverse effect on tuberculous lung lesions, results obtained in this investigation tend to show that therapeutic interruption does not necessarily bring about an improvement in the phthisical condition.

In conclusion the writers are of the opinion that collapse therapy is the sheet anchor for gravidae with active tuberculosis.

To be efficacious this treatment must be instituted early, and routine radiological investigations for all pregnant women should be carried out as a prophylactic measure.

So long as the obstetrician remains unskilled in the technique of collapse therapy, and the physician unfamiliar with modern obstetrical practice, the writers would advocate unified control as outlined in this study.

REFERENCES.

Barnes, H. L., and Barnes, L. R. P. (1930): *Amer. J. Obstet. Gynec.*, **19**, 490.

Cohen, R. C. (1946): *Brit. J. Tuberc.*, **40**, 10.

Jameson, E. M. (1935): *Gynecological and Obstetrical Tuberculosis*, Philadelphia, Lea and Febiger.

McIntyre, J. P. (1948): *Brit. J. of Tuberc.* (In the press.)

Matthews, H. B., and Bryant, L. S. (1930): *J. Amer. med. Ass.*, **95**, 1707.

CEREBRAL VENOUS THROMBOSIS IN PREGNANCY
(A Report of Two Possible Cases)

BY

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THE problem of cerebral accidents in pregnancy and the puerperium has aroused periodic interest since Von Hösslin's (1904) monumental work on the subject. At first there was a tendency to make no distinction between hemiplegia and other manifestations of cerebral damage which occurred before delivery, and those occurring in the puerperium; but of recent years it has been realized that the aetiology is usually different in pregnancy and the puerperium, and the main focus of attention has been upon puerperal cerebral thrombophlebitis. This paper describes 2 cases of cerebral damage occurring in pregnancy, which may have been caused by cerebral venous thrombosis.

Cerebral haemorrhage has always been regarded as the prime aetiological factor in the production of antepartum hemiplegia and aphasia. Von Hösslin describes 12 cases of hemiplegia or aphasia occurring in pregnancy and attributes all of these to cerebral haemorrhage, though in the light of more recent work it is probable that this diagnosis does not explain all his cases. Duhot (1920), reviewing the literature to date, stated that Leclercq (1906) had been able to find only 46 cases of antenatal hemiplegia in his review of the literature, and mentions a further 2 cases of his own. He regarded cerebral haemorrhage, cerebral embolism, and subarachnoid haemorrhage as the 3 main causes in that order of frequency and considered that hemiplegia in pregnancy was not to be regarded as differing aetiologically from hemiplegia occurring at any other time, except in those cases related to toxaemia of pregnancy. Among other rare causes, he mentions cerebral oedema due to toxaemia, the effects of toxaemia on the cortical cells, cerebral anaemia following haemorrhage, syphilitic endarteritis, cerebral tumour and cerebral tuberculoma; he quotes 2 cases where no cause could be found, but he does not mention cerebral venous thrombosis as an aetiological factor. Alpers and Palmer (1929) also consider cerebral haemorrhage to be the most frequent cause, but they refer to 3 cases of cerebral venous thrombosis in pregnancy, 1 of which was associated with an old mastoiditis and responded to treatment of this condition; but in the remaining 2 cases, both of which died, no cause for the thrombosis could be found postmortem.

Sinclair (1902) analyzed 18 cases of "puerperal aphasia" 5 of which occurred during pregnancy. Of these 5 cases, 4 had a hemiplegia in addition to the aphasia, and 3 of these cases had similar symptoms in a subsequent pregnancy. He puts forward the hypothesis that the causative factor in such cases is most likely to be cerebral venous thrombosis. In favour of this idea he notes the increase in fibrin in the blood in the later months of pregnancy when most of these cases occur, the gradual onset of the symptoms, and the liability to recurrence of similar symptoms in a subsequent pregnancy, when vessels which have

been damaged in a previous pregnancy are more liable to be the site of a second thrombosis. Apart from the alterations in blood chemistry, Sinclair gives no suggestion as to why thrombosis should occur in the cerebral veins.

Batson's (1940) work has thrown much light on this. He demonstrated a connection between the pelvic veins and cerebral veins *via* the vertebral system of veins and showed that raised intra-abdominal pressure favoured the transmission of a radio-opaque substance from the pelvic to the cerebral veins by this route. It remains now to find a cause for the pelvic thrombosis.

Martin (1944) states that he has encountered 2 and possibly a 3rd case of cerebral venous thrombosis occurring in pregnancy. In each case the patient had a stillborn child which leads him to suggest that the thrombosis may possibly have occurred first in the placental site.

The 2 following cases, in which a tentative diagnosis of cerebral venous thrombosis was made, differ from Martin's, in that a live child was born in each instance.

Case Reports.

Case 1. Mrs. R. K., aged 29, 3-gravida. First pregnancy 1940, said to be complicated by raised blood-pressure and " kidney trouble " from the 5th month onwards, and labour was induced prematurely on this account, with the birth of a living female child weighing 4 pounds. Second pregnancy 1943, normal throughout with spontaneous full-time labour resulting in a living male child weighing 7½ pounds. Third pregnancy—last menstrual period on 10th September, 1945. First examined on 28th January, 1946, when she was estimated to be 26 weeks pregnant and no abnormality was found except that her blood-pressure was 156/90. The Wassermann reaction was negative. On 22nd February, 1946, the blood-pressure was 160/90. On the morning of 6th March, 1946, the patient's husband found her attempting to move a heavy dustbin. He remonstrated with her and she complained of headache and went to bed. She felt strange and knew that something was wrong but could not tell what. She felt confused and frightened and her eyes would not focus properly. When she reached out her right arm felt strange as if she could not touch things properly. In the afternoon she appeared to have difficulty in expressing herself and in naming common articles and could not recall her children's names. She was admitted to the maternity ward at Mile End Hospital that evening. On admission she was found to be about 34 weeks pregnant, vertex, left occipito-anterior, head not engaged, foetal heart heard, blood-pressure 150/88, urine nothing abnormal found, slight oedema of the ankles. She was quiet and pleasant, smiling when approached and co-operative in the physical examination. She was unable to give any account of herself or of her illness and could not answer simple questions. Sometimes she obeyed instructions correctly, at other times incorrectly. Conversation was limited. " I'm all right. There's nothing wrong with me. I find difficulty in my head. I can't think. I can't quite work it out." She appeared distressed but not agitated. Rough testing of motor and receptive speech functions suggested perseveration, recognition of common objects and their use, but inability to name them. Owing to her aphasia it was impossible to assess how far her orientation and her intellectual functions were impaired. The nervous system was otherwise normal.

As she presented a picture of a confusional state, and no evidence of any serious obstetric complication apart from her raised blood-pressure, she was transferred to the Maudsley Hospital on 7th March, 1946, for psychiatric investigation. The above findings were confirmed, detailed tests of speech function showed nominal aphasia, slight paraphasia, paragraphia and some disturbance of higher conceptual ability. Her recollection of the onset of her illness and of her stay in Mile End Hospital was patchy. X-ray of skull and electroencephalogram showed no abnormality, perimetry showed normal fields, erythrocyte sedimentation rate 58 mm. drop in 1 hour, cerebrospinal fluid normal, urine consistently showed a trace of albumen.

She made slow progress while in hospital, but when re-admitted to Mile End Hospital on 3rd May, 1946, she still had all the above symptoms present

to some degree. She was mildly depressed by her inability to express herself. Physical examination showed the uterus to be at term, vertex, left occipito-anterior, head engaged, foetal heart heard, blood-pressure 144/92, urine nil, abnormal. On 19th May, 1946, she went into labour spontaneously and after 14½ hours was delivered of a living female child weighing 7 pounds 12 ounces. The placenta weighed 2 pounds 2 ounces, and showed numerous areas of infarction, but the nature of these "infarcts" is not stated. Her puerperium was normal and when discharged home on 28th May, 1946, it was reported that her mental state was much improved.

On 9th July, 1947, she attended the out-patient department at the Maudsley Hospital. She stated that she felt very well, her only disability being occasional difficulty in using unfamiliar words: "I know what the word is in my mind but I can't say it." She had a very clear recollection of her illness and remembered many small details of the questions she had been asked. She stated that she did not at first realize that there was anything wrong with her speech but remembers that when she went into hospital she had to answer by signs, and that she could not always understand what was said to her and this made her frightened and confused. Her comprehension and speech had returned gradually and were not complete until some months after the birth of her baby. Her memory appeared to be excellent, she occasionally seemed to have a little difficulty in grasping a question and there was some hesitation over, and mispronunciation of unusual words, e.g. "triang" for triangle and "circe" for circle, but she recognized and named objects correctly and could read and write correctly. She was estimated to have made a very good recovery.

CASE 2. Mrs. E. B., primigravida, aged 32. Last menstrual period 1st July, 1946. Expected date of delivery 8th April, 1947. Pregnancy was normal apart from a cough which necessitated her staying in bed for a few days when 7 months pregnant and which lasted 2 weeks. She also had two or three severe headaches at monthly intervals during the latter part of her pregnancy; these lasted for a whole day and on one occasion the headache was associated with vomiting. She attended the antenatal clinic regularly and no abnormality was noted until 25th March, 1947, when her blood-pressure was found to be 145/90.

The patient gives the following account of her illness. On 25th March, 1947, at about 8 a.m., she had a sudden dead feeling just above her left ankle; there was no weakness and the sensation passed off in about 5 minutes. At about 11 a.m. on the same day, while sitting in the antenatal clinic, she had a feeling of weakness and numbness of her left side in the region of her waist so that she was unable to get up off the bench; this lasted 5 to 10 minutes and passed off. At 7 p.m. the numb feeling in the left leg recurred for a few minutes and then ceased.

On 26th March, 1947, she felt well on rising, but at 9 a.m. she suddenly felt weak and her left side went "dead and stiff". She was unable to move her left arm or leg but could move her right side. She tried to call out but her face felt stiff and she could make no noise. This lasted about half an hour and then wore off, the leg recovering first, then the arm and lastly the face. She telephoned and asked the doctor to call but he did not come that day. At 11 a.m. the attack was repeated, the only change being that her face felt less stiff and she was able to talk; this attack lasted about 20 minutes. There was a further attack at 1 p.m. and from then on small, similar attacks lasting about 5 minutes occurred every 15 to 20 minutes; during these attacks the left side of her face and her left hand twitched. No further attacks occurred after going to sleep but she woke up once during the night with her teeth chattering and her husband had to hold her jaw still till the attack passed off.

On 27th March, 1947, she felt well on first rising but at 8.30 a.m. her left side suddenly became weak, although there were no sensory changes. This weakness persisted unchanged, she could still move and stand but there was a marked difference in power on the two sides. Her doctor visited her and told her that her blood-pressure was raised.

On the 28th March she felt much the same, but while knitting she suddenly lost the use of her left hand so that she dropped her knitting and could not pick it up again.

On 29th March she was admitted to the maternity ward at King's College Hospital. Her admission-notes record pupils equal, discs normal, left-sided hemiplegia, with gross spasticity of arm and increased reflexes, Hoffman's sign positive on

the left, ankle and patellar clonus on the left with left extensor plantar response, no sensory loss. Heart normal. Blood-pressure 150/90.

On 3rd April the patient went into labour spontaneously and after 3 hours had a normal delivery of a healthy male child. There followed a gradual, slight improvement in all the paralyzed muscles except those of the left hand. However, she became very depressed, refused to take any interest in her child and presented a picture of severe, reactive depression; it was felt that she was a suicidal risk and on 11th June she was transferred to the Maudsley Hospital for psychiatric treatment.

On admission she was found to have a left-sided hemiplegia. There was slight weakness of the left side of the face involving mainly the lower half. There was slight ptosis of the left eyelid but eye movements were full and the pupils were equal and reacted to light and on accommodation. The tongue deviated slightly to the left side. There was marked weakness of the left arm, the hand being almost useless, the limb was spastic and the tendon reflexes increased. The left leg was weak, but to a much slighter degree than the upper limb, it was spastic, the tendon reflexes increased, and the plantar response extensor. The abdominal reflexes were absent on the left side. There were no sensory changes. Blood-pressure 130/80, erythrocyte sedimentation rate 4 mm. in 60 minutes, Wassermann reaction negative. Blood count normal, haematocrit, prothrombin, and clotting times normal, icteric index 4, electroencephalogram normal, X-ray of skull and chest negative. She was apathetic and depressed, showing no interest in anything or any desire to get well. She was treated by psychotherapeutic interviews, and physiotherapy directed mainly to increase the use of her upper limb. Two months after admission she had 2 transient episodes in one day consisting of headache, blurring of vision of the left eye and tingling in both hands. These attacks each lasted 10 to 15 minutes and were not accompanied by any abnormal physical signs. When discharged home on 30th September she had almost complete recovery of her facial muscles, much improved power in the leg and improved power in the hand and arm, though fine movements of the hand were still very poor. Mentally she was much more cheerful and ready to help herself.

Discussion.

In both these cases the slow onset of the symptoms suggests a spreading venous thrombosis rather than a sudden cerebral haemorrhage or embolism. In Case 2 the recurrent paresis with Jacksonian attacks may well have been caused by a thrombus which at first only intermittently occluded the orifice of a tributary vein before the whole venous channel became blocked.

The possible diagnosis of disseminated sclerosis must also be considered. The complete and maintained recovery of the first case makes such a diagnosis unlikely. In the second case the development over a few days of a hemiplegia preceded by Jacksonian attacks, with no evidence of any other lesion in the central nervous system, is an unusual picture in disseminated sclerosis. We have now to consider the aetiology of the presumptive venous thromboses in these cases.

There are two factors operating in pregnancy which increase the liability to thrombosis. These are, first, the increased fibrin content of the blood which rises to 40 per cent above normal at term; and, secondly, the slowing of the maternal circulation through the placenta which, with the increased pressure on the iliac veins from the enlarging uterus, leads to stagnation of the blood in the pelvic veins and those of the lower limb. This stasis tends to promote clotting of the blood within the placenta with the formation of degenerative "infarcts" which serve to retard still more the maternal blood flow.

In Case 1 there had been a marked degree of hypertension for at least 5 weeks before her admission to hospital. In view of her previous obstetric history and the subsequent course of her pregnancy, it is probable that this was of the nature of a pre-eclamptic toxaemia. It is known that retroplacental haematomata, similar to

those found in accidental haemorrhage, but usually too small to cause symptoms, often occur in cases of pre-eclamptic toxaemia, and are thought to be due to a sudden relaxation of the maternal arteriolar spasm, with consequent flooding of the capillary bed and rupture of vessel walls. The fact that the patient's placenta was said to contain "infarcts" at term would favour the supposition that such haematomata had in fact occurred. Unfortunately, the term "infarcts" as used in common obstetric parlance is too vague to make this fact certain, as normal degenerative processes are often referred to as "infarcts". Her cerebral accident followed her attempt to lift a heavy dustbin by pressing it against her abdomen and pregnant uterus. It seems possible that this act caused a thrombus from one of the maternal placental veins to be shot off into the vertebral system of veins and thence to the cerebral veins.

The second case is less easy to explain. This woman had a slightly raised blood-pressure by strict obstetric standards, but no more than many women have in otherwise normal pregnancies. The only other abnormality in her pregnancy was the 2 or 3 attacks of severe headache which had occurred and which may have been due to a very limited degree of cerebral venous thrombosis. Her final thrombotic episode was not, however, accompanied by headache. In this patient the only explanation would appear to be to postulate some anatomical or physiological variation facilitating the passage of a thrombus from the uterus to a degree not present in most other women.

These cases show the importance of making an accurate diagnosis at an early stage of the illness. In Case 2, had the condition been recognized at its onset, it is possible that measures might have been instituted to prevent the spread of the thrombosis, with a much less severe development of the illness.

Summary.

The literature dealing with cerebral venous thrombosis in pregnancy is briefly reviewed.

Two cases of cerebral accidents occurring in pregnancy are described, and the factors which lead to the tentative diagnosis of cerebral venous thrombosis discussed. The impossibility of conclusive diagnosis is due to the fact that clinical recovery prevented postmortem confirmation.

My thanks are due to Dr. A. Meyer for much helpful advice and criticism in the preparation of this paper, and to the medical superintendent of Mile End Hospital, and the obstetric department of King's College Hospital, for access to the case records of these patients who were under their care.

References.

Alpers, B. J., and Palmer, H. D. (1929): *J. nerv. ment. Dis.*, **70**, 465.

Batson, O. V. (1940): *Ann. Surg.*, **112**, 138.

Duhot, E. (1920): *Gaz. Hôp., Paris*, **93**, 133.

Hösslin, R. von (1904): *Arch. Psychiat. Nervenkr.*, **38**, 730.

Martin, J. P. (1944): *Proc. R. Soc. Med.*, **37**, 383.

Sinclair, M. A. M. (1902), *Lancet*, **2**, 204.

SOME PRINCIPLES OF MYOMECTOMY*

BY

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"SINCE cure without deformity or loss of function must ever be surgery's highest ideal, the general proposition that myomectomy is a greater surgical achievement than hysterectomy is incontestable." These are the words of Victor Bonney which I choose for my text on this occasion.

Conservative surgical treatment of uterine fibroids presents the enormous advantage, in the case of young women, of permitting the retention of the uterus and its appendages and their consequent function.

The possibility of conservatism has engaged the attention of gynaecologists since the earliest days of operative gynaecology, and Tuffier in France, Alexander in England, and August Martin in Germany, pioneered in the field which was subsequently developed by Victor Bonney.

However, in spite of a wealth of experience together with progress in technique, the operation of myomectomy has nowhere really established itself, no doubt because of the erroneous belief that its mortality is higher than that of hysterectomy. X-ray irradiation, which destroys ovarian function, also is a competitor with the conservative operation because it has no comparable mortality in the postoperative stage.

The principal arguments against myomectomy have been based on—first, the fact that when several fibroid nodules are situated in the depths of the uterine wall, the cavities which result from their removal can become the sites of haematomas, exudates, abscesses—all susceptible to infection. Secondly, that bleeding during the operation and its repercussions in the postoperative stage constitute a further deleterious factor. The third factor is the presumed loss of biological value of the uterus after myomectomy.

That there is a considerable mortality in difficult cases is not always apparent in most statistics, which thus appear more favourable than they are in reality. Therefore, for many gynaecologists, the indications for myomectomy are limited to subperitoneal pedunculated fibroids which offer little trouble and have no mortality-risks. This is borne out by the figures which follow.

Whilst the defenders of myomectomy state that the frequency of its indications are in the ratio of 1:6 or even 1:3 in comparison with hysterectomy, its adversaries put forward the ratio of 1:14 or even 1:20 and suggest that only the desire for pregnancy in the case of young women should be considered as an absolute indication for the conservative operation. The danger of recurrence, which, however, does not surpass a figure of from 3 to 11 per cent, is not enough to outweigh the advantages of the conservative procedure and its importance to the female organism. We know to-day that, when in

* Lecture given at the Chelsea Hospital for Women, London, on 12th June, 1948.

the course of surgical intervention there is no considerable loss of uterine tissue—and, as we will see later on, this can be realized in most cases—the biological value of the uterus remains complete.

Nor does the persistence of certain troubles, and in particular, meno-metrorrhagia, following the operation, constitute an argument against myomectomy, because these inconveniences were reported in old statistics when knowledge of endocrinology was very limited and the therapeutic use of hormones almost unknown.

When meno-metrorrhagia persists after the operation it is due—and biopsies confirm this—to a glandularcystic hyperplasia of the endometrium easily treated by hormones and haemostatics. We also know that, where they exist, follicular cysts, which lead as much to amenorrhoea as to metrorrhagia, can be removed in the course of the operation.

Objections are also based on the probability that future gestation can be expected in about only 14 to 25 per cent of cases. Bonney, however, upholds the view that the function of the uterus remains intact, and furthermore, he has noted later pregnancies in some 38 per cent of cases amongst women from whom even multiple fibroids have been removed. Uterine inertia following delivery, abnormal adherence of the placenta, rupture of the uterus during pregnancy or labour, are rare phenomena which can be blamed, I believe, on the technique employed. Such objections do not, in my opinion, justify the ostracism of the conservative procedure which continues to exist even to-day. They were weighty only in earlier times, when our knowledge of female biology was not as extensive and well-founded as it is to-day, and when surgical technique left something to be desired. But if one considers the aims of conservative surgery of the female genital tract, and the fact that the gynaecologist should be an accomplished surgeon, the conclusion emerges that the reservations which I have enumerated earlier should be abandoned as limiting the field of indications and preventing extension and evolution of the technique.

We should, on the contrary, use all our efforts to minimize the dangers of myomectomy and to allow of its more widespread use, so that the genital system of the young female and, in a more general sense, maternity itself, may be more adequately protected.

My remarks are based on a progressive fall in the mortality-rates in my cases which I propose to report further on in this paper. Such results have allowed me to widen the indications for the operation and to use it systematically amongst all women under 45, independent of the consideration of later pregnancies. One can guarantee in this way the functional integrity of the genital organs or, at least, of the internal ovarian secretion, and this with no increase in the mortality-rate as compared with that of hysterectomy. I would add that the limit of age of 40, which I put forward earlier, I have now raised to 45, following the publication of Terada's statistics showing that in 50 per cent of women with fibroids menstruation continues until the age of 50 years.

Not the great size of a fibroid or the presence of multiple tumours—whose number may sometimes surpass 20—or their situation, or their aseptic trophic changes, or chronic inflammatory adhesions resulting from pressure or from torsion, do I regard as contra-indications to myomectomy. Nor am I concerned with bleeding if it exists at the time when surgical intervention has been decided on.

Temporizing, or any preoperative efforts at treatment (i.e. transfusion) sets up a vicious circle which is to the detriment of

the general state of the sufferer. On occasion I operate on almost exsanguinated women, since this is the only rational method of haemostasis.

It goes without saying that I avoid operating on those with grave cardiac lesions. But the less serious forms of heart trouble, functional murmurs and those reacting favourably to cardiotonic therapy, as well as diabetics controlled by insulin, are quite suitable cases; similarly the obese, in spite of the added difficulties of approach.

I would mention here that with large fibroids, for which one has to have recourse to X-ray irradiation in haemorrhagic cases, where for one reason or another operation is not possible, there is a danger of necrosis. Castration by X-rays brings in its train a diminution of the hyperaemia and nutrition of the tumour, without causing a disappearance of symptoms. I mean that irradiation influences the volume of the fibroid almost only to the extent of inducing a castrational regression of the hyperaemia and oedema. So that pain usually persists and sometimes bleeding, especially when a part of the fibroid is submucous. Further, the reasons which cause us to reject hysterectomy in young women apply even more forcibly to the use of X-rays.

The problem becomes more complex when there is fever which can be due to several causes. If the cervix is open and there is a foul discharge, secondary endometritis can be expected since a submucous nodule diminishes the normal contractility of the uterus and favours the ascent of bacteria into the uterine cavity.

It is clear that in cases of this type, not only myomectomy but all surgical intervention must be postponed until the acute inflammatory process has disappeared. Where there is a submucous nodule it can be removed *per vaginam*. But the possibility of the co-existence of fibroids and pregnancy must not be forgotten, presenting, as it may, similar signs and symptoms and especially bleeding due either to the threat of abortion or to incomplete or missed abortion.

On the other hand, when the cervix is closed and one is satisfied that there is neither endometritis nor other inflammatory condition of the appendages or parametrium (which are absolute contra-indications to intervention), the raised temperature, if any other systematic cause can be excluded, may be attributed to necrosis of the fibroid. The latter does not exclude operative interference since the process following compression or torsion is aseptic.

Here, I should like to draw attention to a point which I think of importance. It is that one should not operate in the presence of a raised erythrocyte sedimentation-rate. This sensitive control indicates, in a manner to which I personally attach an absolute value, that there is or is not, at the moment of operation, evidence of inflammation or acute infection.

I would add that before performing myomectomy, I never use lipiodography. Some workers regard this as an essential for the correct location of the uterine tumours. I think this is of no great importance since the operation is going to be done in any case. On the contrary, when the uterine cavity is shown to be irregular from the presence of fibroid nodules and if one of these to some extent closes the cervical canal, it is possible that the opaque fluid may be incompletely evacuated and thus unpleasant endo- or peri-uterine inflammatory reactions may follow.

I consider that the cervix should be carefully examined before every myomectomy and that, at times, biopsy be

done. One should not lose sight of the fact that cervical cancer together with fibroids of the uterus occur in about 2 per cent of cases, and it goes without saying that in such cases conservative treatment would be disastrous. I think it equally necessary to perform an endometrial biopsy in all cases with bleeding, about 10 days before operation, to avoid missing a co-existent cancer of the body of the uterus. This interval of 10 days is recommended to guarantee the absence of infection.

When first I began to examine, in a systematic manner, the results of myomectomies done by myself, the conclusions were far from encouraging.

When I say " in a systematic manner ", I am not thinking of those relatively easy myomectomies, simple removal of a subperitoneal pedunculated fibroid, or even a small interstitial nodule, such as is commonly dealt with by every gynaecologist. I mean myomectomy in the sense of the excision of fibroid nodules, varying in number and in size, buried in the depths of the uterine muscle and even reaching to the endometrium.

Analysis of my first 100 cases, of which the mortality reached around 10 per cent —almost entirely due to peritonitis—faced me with a dilemma. I could understand the arguments put forward against this conservative operation by the majority of gynaecologists, but, instead of being discouraged, I persevered, believing that I must use my experience to arrive at better results.

As my experience grew, I tried to establish the key features of this operation by examining more than 400 cases; in the last 100 of which my mortality-rate was only 1 per cent.

It seems to me, therefore, that to-day it is worth while publishing the points of technique which led to these results, which I feel to be satisfactory.

It is, in my opinion, a cardinal point that the uterine peritoneum be traumatized as little as possible, and that all the fibroids be removed by a single or, at most, two incisions.

These incisions should be made as high as possible and always transversely. Thus they can be prolonged under the perineum if there are disseminated nodules, either on the anterior or the posterior surface of the uterus, and also transverse incisions present the great advantage that the uterine wounds can be very easily covered, using the uterovesical fold of peritoneum. This is not possible when the incision is either vertical or on the posterior aspect of the uterus. If the attempt were made it would create abnormal anatomical situations of the uterus, necroses, urinary troubles, etc.

Every fibroid should be removed before beginning to suture the resulting cavities. If one closed cavities as they were created, the subsequent removal of other tumours would risk the separation of sutures already placed. Palpation will ascertain whether there remains any tumerous tissue worthy of removal. If any tiny nodules remain undetected it matters little, for which the slow rate of growth of such tumours, they will probably never develop to the point of requiring a second operation until the subject has reached or passed the age of 40 years, when the deprivation of her uterus and ovaries will not be a matter of very great concern to her and total hysterectomy may be done.

There is another reason why all the tumours should be removed before commencing to suture. The needle should not meet fibroid tissue, which does not lend itself well either to suture or to cicatrisation.

It may be said here that those who perform large numbers of myomectomies know that the fibroid degeneration of the

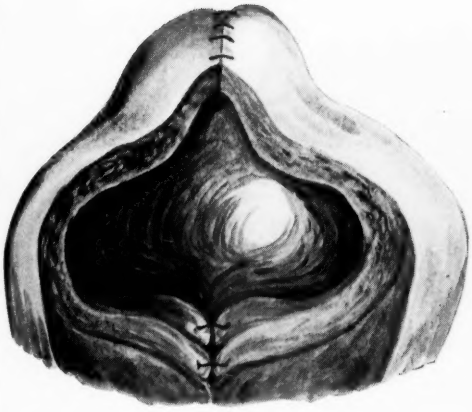

FIG. 1.

The protruding parts of the uterine wall which result after the removal of the fibroid must not be removed but joined together so that they can be inverted and fill the cavity.

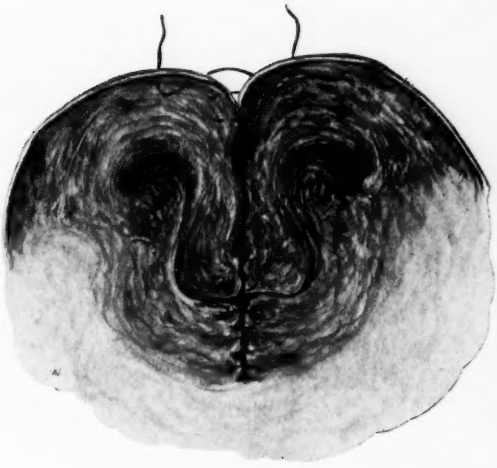

FIG. 2.

The fibroid cavity has been filled with the inverted protruding parts of the uterine wall.

FIG. 3.

The uterine wound has been covered by the vesico-uterine fold, without opening it.

uterine muscle *in toto* is very rare. In such cases, of course, the conservative operation is not indicated. But the overwhelming majority of cases of this complaint are those of fibroid nodules of varying sizes separated from each other by healthy tissue.

A second cardinal point is that of haemostasis, which must be as complete as possible. However, in each cavity left after the removal of a fibroid one only ties bleeding vessels and generalized oozing is ignored, being controlled soon afterwards by the closing of the cavity itself in the way to be described later. It is enough at the time to fill the cavities with small towellings, but never with swabs, which may very well be lost or forgotten.

I, personally, never use the method of controlling bleeding by temporarily clamping the uterine vessels. I think that this leads to danger in that it does not permit local control and for perfect haemostasis one must identify and tie all bleeding points.

Having removed the tumours, one goes on to close the cavities by suturing in successive layers. When two cavities are in close juxtaposition, I do not remove the separating tissue but use it to line the combined cavity space. One should make every effort to avoid opening the endometrium—though this is not always possible—because this slight operative complication is reflected in the resultant statistics. I cannot follow, on this point, those who deliberately open the uterine cavity in order to remove nodules situated on its posterior aspect.

Suturing in successive layers is not, however, the whole story. The chief factor in closing such cavities lies in the *use of uterine tissue itself*, which is done by two continuous sutures. The first of these, which is not tightened, joins the superficial muscular layer with the edge of the wound. The second, which is tightened, joins peritoneum to peritoneum and forces the adjacent and protruding lips of the cavity into its depths. I emphasize this point, which constitutes the main feature of my technique, and which I have not noted elsewhere (Figs. 1 and 2).

For greater security I finish off by some interrupted stitches which run no risk of giving way. But in order that the cavity may be well packed, both from within and without, it must be emphasized, as has been mentioned earlier, that the portion of the uterine wall which protrudes following the removal of the fibroids must not be removed but must be utilized for the above purpose. This manoeuvre has the additional gain of retaining the whole biological value of the uterus, its shape, its volume and its function.

Finally, as an additional measure of security, one employs the peritoneum itself. Even triple suturing, or Bonney's monk's hood, may not be sufficient under certain conditions. Should a haematoma form in the depths of the fibroid cavity and become infected, pus may infiltrate along the sutures and reach the peritoneal cavity. Therefore I use, as I have said above, the vesico-uterine fold (without opening it), not a difficult step, provided that the original incision on the uterus has been made transversely and not far behind the fundus of the uterus (Fig. 3). The suturing of the vesico-uterine fold on the posterior wall of the uterus is sometimes facilitated by Gilliam's operation.*

Thus, all cavities resulting from the operation are completely closed, haemo-

* This fixation of the uterovesical fold on the posterior aspect of the uterus does not affect the normal development of a later pregnancy. Indeed, and even independent of myomectomy, the fixation may prove to be, when the uterus is retroflexed, useful in maintaining an ideal position of the Fallopian tubes after the performance of Gilliam's operation for the cure of sterility. The uterovesical fold distends sufficiently in pregnancy.

stasis is perfect and the traumatized surfaces are extraperitoneal.

There are 2 points of importance in the postoperative phase:

(1) The insertion and retention of an indwelling catheter. This should remain in place for 5 days to avoid the development of pressure by the full bladder on the uterovesical fold and subjacent sutures.

(2) The administration of oestrogens, 50,000 units a day, for 5 days, for the purpose of sensitizing the uterus to the action of pituitary extract and of ergot. These drugs are essential to guarantee the contraction of the uterus and the cavities left by operation.

Elevation of temperature is generally due to the absorption of small haematomas and of the relatively numerous sutures, and this soon falls to normal. When infection is suspected penicillin should be exhibited. But the local use of antibiotics during the operation or prophylactic injections of penicillin are, in my opinion, unnecessary.

Examination sometimes discloses a general enlargement of the uterus which yields quickly to the abdominal application of ice bags. The uterus usually remains for a while somewhat larger than normal and at times there may appear a slight, evil-smelling vaginal secretion containing fragments of the sutures when these have been used on the endometrium. Ergot is clearly at work then.

About the third month following the operation, the uterus assumes its normal size. It retains all its functional value and I have many times learned that the removal of even 10 or 20 fibroid nodules has not prevented a later pregnancy developing normally and going on to a confinement carried out by the natural forces.

The tables show my statistics and emphasize the fall in the mortality rate which has come about with experience.

MYOMECTOMY RECORDS (PERIOD 1932–1948)

Total number	400
Mortality	17
Mortality rate (per cent)	4.25
Morbidity rate (per cent)	18.59
Simple Myomectomy	364
Mortality	15
Mortality rate (per cent)	4.12
Myomectomy + pregnancy	36
Mortality	2
Mortality rate (per cent)	5.55
1st period (1932–1942)	184
Mortality	13
Mortality rate (per cent)	7.06
2nd period (1942–1948)	216
Mortality	4
Mortality rate (per cent)	1.85
Uterine cavity opened	52
Mortality	13
Mortality rate (per cent)	9.61
Uterine cavity not opened	312
Mortality	10
Mortality rate (per cent)	3.20

	Per cent
1st 100 cases—mortality rate	10
2nd ,, ,,	4
3rd ,, ,,	2
4th ,, ,,	1

Number of Fibroids in each Case	No. of cases
1 Fibroid	181
2–5 Fibroids	131
5–10 ,, ,,	20
10–20 ,, ,,	11
20–39 ,, ,,	12

Size of Fibroids	No. of cases
Small (walnut)	42
Medium (orange)	180
Large (foetal head)	180
Enormous (bigger than foetal head)	33

This improvement I attribute to following the principles described above and which have been established by experience. Therefore I wish to recommend them to others who will employ them, develop them and control them, and thus crystallize a technique allowing a much wider use of an operation designed to conserve the female reproductive organs and their function to the end that they may enjoy, in the phrase of Victor Bonney "the fruits of conservatism".

THE CARE OF THE EYES AT BIRTH

BY

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AND

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IT has been felt by many workers that the use of silver nitrate as a prophylactic for ophthalmia neonatorum was due for review. These strongly caustic astringent drops may have a place in a practice where the commonest cause of infection is the gonococcus, but their use otherwise is open to question.

It has also been suggested that the silver nitrate itself has been responsible for some cases of "sticky eye", and that its use predisposes to infections. Some other agents which have been used are acriflavine in oil, mercurochrome (Marin-Amat, 1936), Protargol (Ballantyne, 1936), silver acetate, Sophol (Stein, 1917), and penicillin (Franklin, 1947).

This investigation was undertaken to decide if silver nitrate did, in practice, cause chemical irritation, if it prevented infection other than gonococcal, and to obtain some indication of the desirability or otherwise of continuing the use of Credé's method.

PROCEDURE.

As a preliminary, the normal flora of the baby's eye was investigated by cultures taken at just after birth, at 48 hours, and at a time some 7 to 10 days later. All babies had the eyes cleansed with a swab immediately after birth. These infants then received the standard prophylactic drop of 1 per cent silver nitrate into each eye on transfer to the lying-in ward. The first culture was taken before these drops were administered. In the main investigation the male babies received silver nitrate, and the female babies no drops at all. Only babies born during the day had bacteriological examinations.

BACTERIOLOGICAL METHOD.

Cultures were taken from the right and left conjunctival sac by drawing a sterile platinum loop along the lower fornix. This was then inoculated on blood agar and chocolate agar plates. The plates were incubated aerobically for 24 hours, and any growth was examined as a Gram-stained film as well as morphologically. *Staphylococcus aureus* was only reported where the coagulase test was positive. All β-haemolytic streptococci isolated were grouped.

Cases of "sticky eyes" and conjunctivitis occurring in the hospital were also investigated. A "sticky eye" was diagnosed when a definite purulent discharge, however slight, was present.

The laboratory procedure was similar in these cases, except that wool swabs were sent to the laboratory instead of plates being inoculated at the bedside. Films stained with Gram, and where necessary,

with Giemsa were examined in all these cases.

Results.

The organisms found did not in general present any unusual features. The gonococcus was not isolated in any case, but this was not unexpected, since only 1 case of gonorrhoea in the mothers occurred during the period. *B. proteus* was isolated from 1 case and its repeated isolation from a child with a rather chronic conjunctival irritation would suggest that it was the causal organism. All cases of infection with *Ps. pyocyaneus* occurred within a limited period, and some were associated with a discharging ear, from which the organism was also isolated. There were, during that time, adult patients from whom *Ps. pyocyaneus* was isolated.

In the cultures taken immediately after birth, it was striking that in very few instances were any organisms isolated. The cultures were taken before the babies were bathed. In all, 6 out of 340 showed growth on first culture, and none subsequently developed eye infections. We therefore feel confident that for practical purposes these babies' eyes could be regarded as sterile at birth. The organisms are shown in Table I.

The number of male and female children, and the numbers of babies from whom organisms were isolated in each group is shown in Table II. Many of these cases did not become clinically infected, although with a positive culture.

Table I.

Organisms in First Swabs.

Left:	*Right*:
Diphtheroids.	Coliform bacilli.
Sterile	Coliform bacilli.
Group B. haemolytic streptococci.	Group B. haemolytic streptococci.
Staph. aureus, albus, Group B. haemolytic streptococci and coliform bacilli.	*Staph. aureus.*
Sterile.	*Staph. aureus.*
Sterile.	*Staph. aureus.*

Table II.

Treated and Untreated Groups.

Male "treated" children—102,
of whom 18 showed growth on culture.
Female "untreated" children—118,
of whom 19 showed growth on culture.

Rate of infection:
Male 17.6 per cent.
Female 15.4 per cent.

It will be noted that the infection-rates are very similar in the 2 groups.

The incidence of infection with different organisms, shown in Table III, was similar in both the clinical cases and the cases used in the experiment. The organisms isolated are similar to those found by Sorsby and his colleagues (Sorsby, Hoffa and Smellie, 1942; Sorsby and Hoffa, 1944), except that we had no cases of gonococcal ophthalmia.

Table III.

	Preliminary investigations	Infants		Clinically infected eyes
		Males	Females	
Staph. aureus	18	16	12	51
Staph. albus	–	1	1	5
Haemolytic streptococcus (B)	1	–	4	1
Strep. viridans	–	2	–	2
Non-haemolytic streptococcus	–	–	–	–
Ps. pyocyaneus	–	–	–	3
Micrococci	2	–	4	2
Coliform bacilli	1	–	1	2
Diphtheroids	–	1	3	–
B. proteus	–	–	–	1
	22	20*	25†	67

* Two cases of different organisms on different occasions.

† Six cases of different organisms on different occasions.

TABLE IV.

Cases with more than one organism.

	Infected eyes
Staph. albus and diphtheroid	2
Staph. aureus and diphtheroid	4
Non-haemolytic streptococcus and *Staph. aureus*	1
Staph. aureus and *Staph. albus*	2
Staph. aureus and *Ps. pyocyaneus* ...	2
Staph. aureus and coliform bacilli ...	2
Staph albus, Staph. aureus, coliform bacilli and streptococci	1

The figures in Table IV represent the number of children infected with each organism. An organism has only been counted once from any one case. Repeated isolations from the same case have not been counted. The clinically infected babies included most of the cases occurring in the hospital during the period of the investigations.

It is interesting to compare the frequent occurrence of *Staph. aureus* in our and Sorsby's cases with the paper of Thomas (1928) in which he reports as a rarity 100 cases of *Staph. aureus* infection in the neonatal period.

Our results do not follow those of Browning (1936), who obtained a high percentage of pneumococci. He also attributes purulent cases, in which organisms were not found, to irritation by silver nitrate. We do not consider, however, that examination of pus by methylene blue and Gram-stained films is adequate to prove the absence of organisms or inclusion bodies.

TREATMENT.

Until penicillin was available sulphonamides, locally or systemically were used in the treatment of infected eyes. Local albucid drops have now been given up. The administration of sulphamezathine or sulphathiazole orally for 2 to 4 days accompanied by local cleansing has been found effective in most cases.

Penicillin has also been used both locally and systemically. We have used it in accordance with the technique described by Sorsby (1945) and Sorsby and Hoffa (1945) one drop of solution of 2,500 units per ml. being instilled at frequent intervals for 1 to 2 hours. Sometimes this has had to be repeated on several days. This is an effective treatment, but requires one nurse's entire attention. Systemic penicillin, as now recommended by Sorsby (1947) either in 2 large doses daily, or in smaller, more frequent injections has been found more reliable and is less likely to involve handling of infective material. Frequently the discharge clears after the first injection.

It is probable, however, that oral penicillin in adequate amounts will supersede the above methods.

The treatment has always been started in advance of bacteriological diagnosis, and has been modified subsequently if necessary.

CONCLUSIONS.

There does not appear to be any great difference in the infection rate between "treated" and "untreated" eyes. No clinical evidence is found for an irritative conjunctivitis due to silver nitrate. In this we do not agree with the findings of Franklin (1947) who found that, of infected eyes, 3 times as many occurred in babies receiving silver nitrate as in those receiving penicillin drops.

Our results add support to the view that silver nitrate is not harmful in itself when carefully administered. The importance of fresh solutions, and strict adherence to the correct dosage have been frequently stressed.

On the whole, however, it does not appear that, in the type of case encountered in this hospital, the use of silver nitrate is

still necessary. The adequate treatment of gonorrhoea in the mother, and the availability of potent therapeutic agents for its treatment in the child have probably rendered the administration of any form of eye drops unnecessary.

Our thanks are due to Dr. J. Murray, Director of the Bernhard Baron Memorial Research Laboratories, for advice and encouragement; to the medical staff for permission to carry out the investigation; and to Mr. Goodwin for technical assistance.

One of us (M. D. T.) is receiving a grant from the Nuffield Foundation, and is working under the direction of Professor Alan Moncrieff, Director of the Institute of Child Health.

REFERENCES.

Ballantyne, A. J. (1936): *Trans. ophthal. Soc. U.K.*, **56**, 46.

Browning, S. H. (1936): *Trans. ophthal. Soc. U.K.*, **56**, 24.

Franklin, C. H. (1947): *J. Amer. med. Ass.*, **134**, 1230.

Marin-Amat, M. (1936): *Trans. ophthal. Soc.* U.K., **56**, 38.

Sorsby, A. (1945): *Brit. med. J.*, **1**, 903.

Sorsby, A. (1947): *Brit. med. J.*, **2**, 322.

Sorsby, A., and Hoffa, E. L. (1944): *Brit. med. J.*, **1**, 353.

Sorsby, A., and Hoffa, E. L. (1945): *Brit. med. J.*, **1**, 114.

Sorsby, A., Hoffa, E. L., and Smellie, E. W. (1942): *Brit. med. J.*, **1**, 323.

Stein, I. F. (1917): *Ann. Ophthal.*, **26**, 411.

Thomas, A. B. (1928): *J. infect. Dis.*, **43**, 306.

BREAST HYPERTROPHY AND PREGNANCY

BY

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DURING the last 5 years I have had the opportunity of operating on 6 patients suffering from excessive hypertrophy of the mammary glands. Because of the unusual symptoms that each of these cases presented, and the similarity of the pathological condition, I have been urged to write this paper.

Primarily I was concerned with the plastic reduction of the hypertrophy of the breasts of these patients, each of whom was suffering from either habitual abortion or sterility. The remarkable results, however, that followed surgical intervention brought me to the conclusion that there exists a connexion between breast hypertrophy and the course of pregnancy. I am quite aware that the material upon which I draw my conclusions is not sufficient, yet the consistency in all cases warrants attention and cannot be dismissed as pure coincidence.

Four of these patients were suffering from habitual abortion. All were between the ages of 25 and 35 years, of normal build and enjoying general good health. They were married to normal, healthy men and, although no pathological condition could be found, the patients presented a history of recurrent abortion between the 3rd and 4th month of pregnancy. All 4 patients had been under the constant supervision of a gynaecologist and had undergone all necessary precautionary treatment, particularly avoiding all mental and physical strain. In spite of this, uterine contractions and haemorrhage invariably occurred after the 3rd month of pregnancy, resulting in complete abortion during a period of 2 to 3 weeks.

Three of these women were curetted before their last pregnancy to no avail. Two presented similar states of health and mental outlook and, although no pathological condition could be detected, they were sterile. Both had been married 5 years; one reported an occasional delay in her menstrual periods, followed by an excessive loss of blood, which pointed to a definite glandular disturbance if not to an early abortion.

The similarity in all cases was an excessive hypertrophy of the breasts, and the surprising results of surgical intervention were that each patient became pregnant after the plastic reduction of the mammary glands. Five completed normal pregnancy and were delivered of healthy children. The last, on whom the operation was performed 6 months ago, is now in the 4th month of pregnancy, and there are no signs of threatening abortion.

CASE HISTORIES.

CASE 1, February, 1942. D. H., 29 years of age, married to a dentist. Family and personal history normal. The patient is the 4th child in a family of 6, the husband the 2nd child in a family of 3. The patient started menstruating at the age of 14. By the age of 18 she had already developed excessive breast hypertrophy, which was a cause of great embarrassment and suffering to her. Married at 22, reporting normal sexual life. First pregnancy occurred soon after marriage and progressed normally for 3 months. After the 3rd month

she gradually began to experience abdominal pain and slight loss of blood. Threatened abortion was diagnosed by the gynaecologist and, although all necessary precautions were taken, the patient miscarried 10 days after the beginning of the symptoms. This was followed in the course of time by 3 more pregnancies, with the same results. I was called into consultation by the gynaecologist after the patient had received hormonal treatment without much benefit.

On examination, the patient presented excessive hypertrophy of both breasts, which were painless on palpation. Plastic reduction was decided upon. I removed three quarters of the glandular tissue in a one-stage operation. Post-operative treatment was normal and the patient was discharged from hospital 3 weeks later.

Four months after surgical intervention she became pregnant for the 5th time. She was kept under constant supervision by the gynaecologist, but no special precautions were taken. Pregnancy developed normally and she was delivered of a healthy boy, 8 pounds in weight. There were signs of lactation in the breasts, but the quantity of milk was not sufficient to warrant feeding the baby. The patient has since been delivered of a further child.

Case 2. September 1942. S. R., aged 31 years, married for 7 years to a healthy mechanic. Personal history of both husband and wife normal. Patient started menstruating at the age of 12, and stated that up to the age of 21 she had normal-sized breasts. Married at the age of 24. First pregnancy occurred 3 years after marriage, by which time she had put on flesh and her breasts had developed excessively. To avoid repetition I will only mention that the history is similar to Case 1. The patient became pregnant 3 times and aborted about the 3rd month for no apparent reason. She visited the gynaecologist at regular intervals but the results were always the same.

Plastic reduction, with the removal of two-thirds of the glandular tissue, was carried out. The breasts were left slightly larger than the previous case in order to conform to the general physique of the patient. She remained sterile for over a year after the operation, despite living a normal married life. The fourth pregnancy occurred exactly 15 months after the operation and progressed normally. She was delivered of a healthy boy. The child was 9 pounds in weight and delivery was by forceps. In March, 1946, she was delivered normally of a baby girl.

Case 3, June 1943. H. W., 27 years of age, married for 4 years; husband of poor physique, a bank clerk. Both husband and wife reported normal family histories. Wife became pregnant 2 months after marriage and progressed normally for 4 months. Onset of pain and haemorrhage was sudden and for no apparent reason. Complete abortion occurred in the course of 8 hours from beginning of symptoms. On 2 more occasions patient became pregnant, with abortion occurring during the 4th month. No pathological condition whatsoever could be found, with the exception of excessively large breasts which, the patient stated, had developed very quickly since puberty. Her menstrual periods had been slightly irregular. After the 3rd abortion the patient was curetted and 2 weeks later plastic reduction of the breasts was carried out. Three-fourths of the breast tissue was removed. The patient was seen again 3 months later and was found to be 2 months pregnant. Pregnancy terminated normally with the birth of a baby girl. She again became pregnant during the following years and was delivered of 3 normal children. After birth of the last child she was advised to use contraceptives on account of a weakened state of health.

Case 4. January 1944. B. D., 34 years old, of slim build and narrow pelvis. Married for 10 years to a healthy professional soldier. Personal and family histories normal. For financial reasons the couple had avoided having children during the first 5 years of their married life. In the last 4 years the patient became pregnant 3 times and aborted each time during the 3rd month of pregnancy. No abnormality was found apart from the narrow pelvis, which was believed to be the cause of the abortions. The patient, however, had abnormally large breasts, which appeared almost grotesque in comparison with her slender frame.

Plastic reduction with removal of almost the entire gland was performed. She became pregnant a few months later and the pregnancy proceeded normally for 8 months; at this stage she became very uncomfortable with the pressure of the pregnant uterus on the internal organs—due to her small build. Caesarean section was deemed advis-

able and was performed 3 weeks before term. A small 5½ pounds baby girl was delivered. Post-operative recovery was normal. The patient was allowed to have another child which was delivered by Caesarean section and at the same time she was sterilized as it was considered that further pregnancies would endanger her health.

CASE 5. March 1944. S. C., aged 27 years, of normal build and health. Nothing of note in personal and family history. Began menstruating at the age of 15 and by the time she was 21 her breasts were abnormally large, which not only caused her much embarrassment but interfered with her favourite sport of swimming. She married at the age of 20 and, although enjoying normal marital life, no pregnancy occurred. Both husband and wife had been medically examined, but no cause could be found for the sterility and several courses of treatment had been prescribed and carried out without beneficial result. The absence of a child was threatening their happiness.

Plastic correction of the breasts was carried out primarily for aesthetic reasons, but the possibility that the intervention would help to cure the sterility was not overlooked. Six months after the operation the patient was examined and found to be, apparently, in the 4th month of pregnancy. Because of the somewhat abnormal appearance of her condition, she was kept under constant observation for the next few weeks. By this time slight haemorrhage had occurred and the size of the abdomen did not correspond with the age of the pregnancy. An X-ray examination demonstrated the presence of a hydatidiform mole. Evacuation of the uterus was performed by the abdominal route. For a year the patient adopted the use of contraceptives because of the state of her health, after which period she was allowed to become pregnant and was delivered of a normal boy.

CASE 6. September 1947. P. G., aged 25 years, a very healthy well-built woman. Family and personal history of both husband and wife showed nothing abnormal. Patient began menstruating at the age of 12 and already at that time she had developed unusually large breasts. Married at 19, and had no pregnancies for the first 6 years. She reported that her menstrual periods had occasionally been delayed, sometimes for as long as 10 days, and were then followed by a heavy loss of blood. These could be interpreted as early miscarriages.

Encouraged by the success of a previous case, plastic reduction of the breasts was recommended as a remedy for sterility. The mammary glands were reduced to one-fourth their size. Four months after the operation the patient became pregnant and in April 1948 she was found to be in the third month of pregnancy. She is being kept under regular observation and there is every reason to believe that the pregnancy will continue to term without complications.

CONCLUSIONS

From the above cases I am convinced that there exists a connexion between breast hypertrophy, habitual abortion and sterility in women. The similarity of the six cases cannot be dismissed as pure coincidence. In all cases I have operated on I have applied a personally devised technique for breast reduction. This consists of removing the outer two-thirds of the glandular tissue, leaving the inner one-third which is supplied with blood by the internal mammary artery. At the same time the skin incision is placed in such a way as to leave only one small vertical scar below the nipple. This technique has the advantage of being adaptable for any degree of hypertrophy and allows the surgeon to execute the breast reduction in about 2 hours.

Although these cases may not be conclusive evidence, still they are sufficient to warrant further research into the causes of sterility and habitual abortion when no other pathological condition exists apart from the enormous size of the breasts. In these cases the operation not only cured the sterility and habitual abortion, but in reducing the breasts to normal size improved the general health of the patient and her physical appearance. The psychological benefit derived from the operation cannot be overlooked.

Naturally, one cannot emphasize too

strongly that not all women with oversized breasts would be sterile or subject to habitual abortion. There are hundreds of normal and fertile women who have overdeveloped mammary glands. It is only in cases of proven sterility and when all other treatments have failed to help the women to become pregnant that one may consider hypertrophy of the breast as the cause of sterility. The operation is suggested as a last resort.

These results also prove the error of the idea that plastic intervention of the mammary glands leads to subsequent inability to lactate, and also interferes with the normal mission of woman to bear children. On the contrary, the reduction of oversized breasts serves to encourage normal pregnancy and cures sterility. Moreover, the inability to lactate cannot be due to the operation as greatly hypertrophied mammary glands are, as a rule, physiologically incapable of function.

The most feasible explanation of the connexion between hypertrophy of the breasts and habitual abortion and sterility is the action of the mammary gland hormones upon the pregnant uterus. It would seem obvious that an enormous breast produces an abnormal quantity of hormone, which by the 4th month reaches saturation, thus stimulating the fibres of the myometrium and causing them to contract. This hormonal saturation in the patient with normal breasts is reached only in the 9th month of pregnancy. The possibility also arises of the same phenomenon occurring in premature births. Finally, the hormonal action on the uterus can be either direct or indirect by means of other endocrine glands, particularly those that are involved in facilitating and maintaining a normal pregnancy.

From this short exposition one realizes that systematic research is needed in order to establish as certain the connexion between hypertrophy of the breast, abortion and sterility. It might be possible to isolate a specific hormone from the breast tissue which exists only in mammary hypertrophy and which is the cause of sterility. I sincerely hope that some better equipped research workers will take up this study and furnish the proof, which I believe exists, of connexion between the two conditions.

A CASE OF ELEPHANTIASIS VULVAE

BY

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THIS case is considered to be worth recording because of the unusual aetiology of a tumour of the external genitalia which necessitated two deliveries by Caesarean section.

Elephantiasis vulvae is a term which one usually associates with tumours found in tropical countries and ascribed to filariasis due to *Wuchereria bancrofti*. In temperate climates, the disease is known as elephantiasis nostras and is usually the result of lymphatic stasis due either to chronic ulceration and fibrosis, or to the pressure of a neoplasm. The term elephantiasis, however, is often loosely given to any swelling of the vulva due to lymphatic or venous stasis, even though this may resolve as a result of treatment.

After studying the literature on this subject one concludes that true elephantiasis is not only an oedematous condition caused by lymphatic stasis, but that there is also a fibromatosis or hypertrophy of the underlying connective tissue. Lymphatic stasis itself, which may be due to varied causes, is an essential step in the development of the disease but, according to Witherspoon and McFetridge (1933), the hypertrophic changes in the underlying connective tissue do not occur until an infection of some sort has been superimposed.

In filariasis, elephantiasis is a clinical manifestation of the disease and is due primarily to obstruction of the lymphatic channels. Anderson (quoted by Manson, 1946) is of the opinion that bacterial infection by staphylococci and streptococci is invariably associated with the disease, and it can well be imagined that the cutaneous ulcers commonly found on the surface of these swellings are readily available portals of infection. It has long been emphasized by authorities on tropical medicine that elephantiasis often results from repeated bacterial infection of the lymphatic system, which has already been damaged by the filarial worm. Repeated invasions by the filariae themselves are not essential, and dead or calcified filariae, acting as foreign bodies, may be enough to keep alive a chronic low-grade infection. Suarez (1933) declares that although filariae may be the cause of the lymphatic obstruction in many cases, all patients sooner or later become the victims of bacterial invasion and that the rôle of infection is a *sine qua non* in the formation of elephantiasis. These points are relevant in this case, the history of which follows.

CASE HISTORY.

The patient, a married woman now aged 25, has borne 4 children. The first in 1942 was a normal delivery, the perineum remaining intact. In August, 1944, after a normal delivery at term in another hospital, there was a perineal laceration requiring two silkworm-gut sutures. These were removed on the 7th day, but when the patient went

FIG. 1.
The tumour lying in its natural position and occluding the introitus.

FIG. 2.
Showing involvement of the left labium minus only.

FIG. 3.
Showing the infected sinus on the outer aspect of the left labium majus.

A.M.

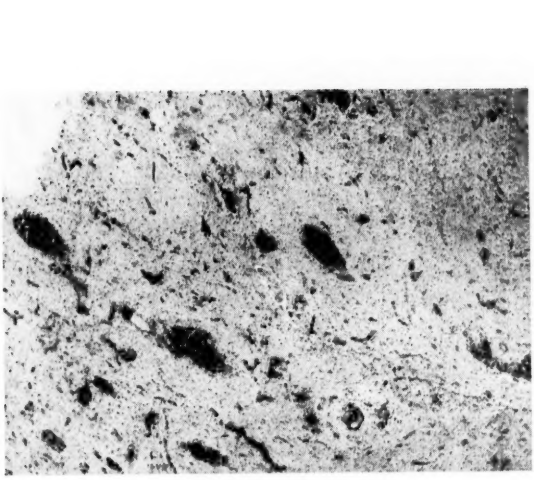

FIG. 4.

Section showing oedematous collagen traversed by vessels with perivascular collections of lymphocytes and plasma cells.

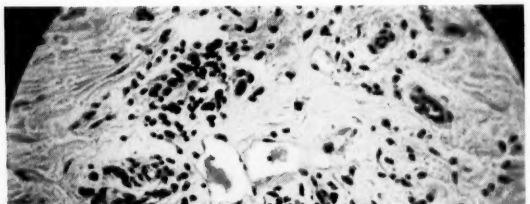

FIG. 5.

High-power view showing inflammatory perivascular infiltrations and two dilated lymphatic vessels.

to the toilet, she felt something pricking her. This was found to be a piece of silkworm gut and was removed. About a month after leaving hospital the glands in both the woman's groins became enlarged and " pus poured from the 4 stitch holes" in her perineum, particularly from the left side. She reported this at the postnatal clinic, and the condition apparently cleared up with treatment. She again became pregnant in March, 1945, but in June a painful swelling developed in the left labium.

On 27th July she made her first attendance at this hospital's antenatal clinic. She was found to have a warty, irregular swelling of the left labium minus, about the size of a small orange, of doughy consistence and slightly tender. There was a contact ulcer on the inner surface of the swelling, and bilateral, small, discrete, painless inguinal glands were noted.

She was admitted to the antenatal ward as she was thought to have blocked lymphatics due to a chronic Bartholinitis. The Wassermann reaction and Kahn test were negative, the gonococcal complement fixation test was negative and no infiltration was detected on X-ray of the chest. Culture of the vaginal swab gave a growth of *staphylococcus aureus*, and from the vulval ulcer a small growth of *staphylococcus albus* and diphtheroids was obtained. She was given a course of sulphanilamide and penicillin, and on discharge from hospital the swelling was definitely smaller.

She attended the antenatal clinic regularly until 21st November, when she was readmitted to the antenatal ward, and given a further course of penicillin. The tumour, which had enlarged once more, was suspected to be due to a retained suture.

On 28th November, the patient went into labour and was delivered of a male infant, weighing 7 pounds (3,178 g.), by lower uterine segment Caesarean section. The puerperium was uneventful, but at the postnatal clinic a new indurated area was noted between the left labium majus and the groin. The woman was referred to the gynaecological out-patient's department as it was considered that the tumour should be excised, but she failed to attend.

On 13th December, 1947, she reported to the antenatal clinic when 32 week's pregnant. The elephantiasis of the left labium minus was noted, and she was recommended to wear a T-bandage for support. During subsequent visits, it was seen that the tumour had so increased in size as to preclude delivery *per vias naturales* and it was therefore decided to admit her at the 36th week for rest prior to delivery by Caesarean section at term.

On 12th January, 1948, she was admitted to the antenatal ward and her general health was found to be satisfactory. The height of the fundus corresponded to 38 weeks' gestation and the position of the vertex was left occipito-anterior. The Wassermann reaction and Kahn test were again negative. The erythrocyte count was 4,400,000, the haemoglobin 74 per cent, and the white-cell count 7,700. The differential count showed neutrophils, 71 per cent; lymphocytes, 27 per cent; large mononuclears, 2 per cent. There were no eosinophils.

On 21st January she was delivered of a female infant, weighing 6 pounds 10 ounces (3,000 g.) by lower uterine segment Caesarean section. The puerperium was uneventful.

On 25th May she was admitted to the gynaecological ward. Her general condition and lactation were satisfactory. Examination of the external genitalia showed a large, warty painless swelling of the left labium minus, about the size of a tangerine, which was fleshy in consistence and did not pit on pressure. There was an old sinus about ½ inch (1.2 cm.) in length on the outer aspect of the left labium majus, with a red indurated area above and below. The left inguinal glands were enlarged and painful and there were also a few small, shotty glands in the right groin. No other abnormal physical signs were noted.

On culturing a swab taken from the sinus, there was a moderate growth of congulase negative *staphylococcus albus* and *diphtheroid bacilli*. The blood sedimentation rate showed a fall of 15 mm. in an hour. The erythrocyte count was 4,100,000 the haemoglobin 78 per cent, and the total white-cell count was 7,000. The differential count was neutrophils, 50 per cent; eosinophils, 2 per cent; lymphocytes, 44 per cent; and large mononuclears, 4 per cent. There was no growth on culturing a catheter specimen of urine and a vaginal swab.

The patient was given a prophylactic course of 1,400,000 units of penicillin and sulphamezathine 11 g., prior to operation on 2nd June.

Under general anaesthesia, an elliptical incision was made around the base of the tumour, which was then dissected out. A probe was passed into

the sinus on the outer aspect of the left labium majus and an incision made down on to the probe. There was a fibrous track and in it was lying a piece of silkworm gut which measured 4 cm. (1.6 inches). The track was excised and the skin edge of the sinus was scarified. The musculofascial layers were approximated with interrupted No. 2 catgut sutures which controlled bleeding effectively, and the skin edges were united with interrupted silkworm gut sutures. A drain was not inserted.

The wound healed satisfactorily, as did the opening to the sinus. There was no haematoma. Recovery was uneventful and the patient was discharged on the 15th June.

The pathological report on the tumour was as follows:

"A mushroom-like mass 6 by 4.5 by 4.5 cm., consisting of soft boggy connective tissue and covered by a thick corrugated skin. Histologically the overlying skin is keratotic. The mass consists of well-formed, rather oedematous collagen. This is traversed by arteries, veins and nerves and contains a little elastic tissue. Around the arteries there are frequent focal collections either of lymphocytes or plasma cells (but never both). There are frequent wide vascular channels which are devoid of red cells and appear to be lymphatics. These often contain hystiocytes and sometimes giant cells. The appearances as a whole are typical of elephantiasis and are consistent with lymphatic blockage."

On 14th July, on re-examination, the wound was found to have healed satisfactorily and there was no tenderness on pressure. The patient had not started to menstruate as she was still nursing her infant.

Commentary.

Tuberculosis, syphilis, gonococcal infection and parasitic disease were excluded as of aetiological significance in this case. There is no doubt that the retained piece of silkworm gut was the prime aetiological factor. Lymphangitis and lymphadenitis following the "stitch abscess" led to a sclerosis of the inguinal glands with resultant oedema of the labium. Chronic irritation caused by the retained silkworm gut at the base of the small sinus infected with *staphylococci* and diphtheroid bacilli helped to keep alive a low-grade infection. The two most important factors in the causation of elephantiasis, according to the literature, were thus present in this case, oedema caused by obstruction of the lymphatic vessels and a superimposed bacterial infection.

I would like to thank Professor J. Young for his help in presenting this case.

References.

1. Anderson, quoted in Manson's *Tropical Disease* (1946), 12th edition, page 718.
2. Suarez (1933): Quoted in Stitt's *Tropical Diseases* (1945).
3. Witherspoon and McFetridge. (1933): *Amer. J. Obstet. Gynec.*, **26**, 84.

INTESTINAL OBSTRUCTION IN PREGNANCY

BY

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INTESTINAL obstruction is a rare but serious complication of pregnancy. The incidence is variously assessed at between 1 in 7,000 and 1 in 68,000 pregnancies. Smith and Bartlett (1940) found 1 case amongst 66,431 deliveries in the Boston Lying-in Hospital, while Bemmis (1932) records that the complication arose twice in a review of 15,000 obstetric cases at the Women's Hospital, New York. In the early part of this century the German literature contained many references to the subject, and in 1913 Ludwig collected 95 cases (Table I). At the Postgraduate Medical School of London during the past 12 years there has not been a single case until recent months, when this abdominal catastrophe occurred on 2 occasions—giving an incidence of 1 in 12,000 pregnancies.

DISTRIBUTION IN RELATION TO PREGNANCY.

There has been considerable controversy regarding the period in pregnancy when obstruction is most likely to occur. Both Ludwig (1913) and Mikulicz-Radecki (1926) suggest the following incidence:

(*a*) During the 4th and 5th month when the uterus ascends from the pelvis.

(*b*) During the 8th and 9th month when the foetal head descends into the pelvis.

(*c*) During delivery and the early puerperium when there is a marked change in the size of the uterus.

However, of the 2 cases we record in this paper, one occurred at the 28th week and the other at the 12th week of pregnancy.

Age incidence. There appears to be no maximal age-incidence at which the complication may arise—indeed it can occur at any time in the child-bearing period of life. One of our patients was aged 16 years and the other 34.

Aetiology. Textbooks (e.g. Titus, 1937) suggest that any factor known to cause intestinal obstruction in the non-pregnant patient may similarly complicate pregnancy. The word "similarly" is misleading, however, for while it is possible for any or all of these factors to play a part in the production of obstruction in pregnancy, sufficient stress has not been placed on the importance of certain of the factors and the relative unimportance or rarity of others.

In classifying the aetiology of acute or chronic intestinal obstruction it is convenient to use the following headings.

(*a*) *Extramural.* In this group herniae, adhesions and adhesive bands must be considered.

Cope (1940), in a study of 301 consecutive cases of intestinal obstruction in the non-pregnant patient, found that in 55 per cent the aetiological factor was strangulated hernia. A study of Table I shows that in Ludwig's series of obstruction in preg-

nancy, 7 per cent were the result of herniae, while Eliason and Erb (1937) recorded only 2 such cases or 3 per cent. This low figure has been observed by other authors. Hernial strangulation, therefore, would appear to be relatively rare, no doubt due to the mechanical effect of the enlarged uterus pushing the bowel away from the femoral and inguinal areas. For For the same reason, obstruction of an umbilical hernia would be rare after the 16th week of pregnancy; yet strangulation of an incisional hernia in the upper abdomen might occur at a later period, the possibility diminishing up to the 36th week, and then increasing during the last month of pregnancy, when the uterus descends into the pelvis. Incisional herniae occur with increasing frequency towards the pubis and are comparatively rare above the umbilicus (Bonney, 1944), providing an additional reason for the relative infrequency with which this type of hernia causes obstruction in pregnancy. In passing, however, it would seem reasonable to argue that while the probability of strangulation of the various types of herniae we have mentioned largely diminishes with the growth of the uterus, the rising fundus should enhance the possibility of a loop of intestine passing into a peritoneal recess within the abdominal cavity—especially into fossae about the duodenum or into congenital defects of the diaphragm. Fortunately such defects are extremely rare.

As Table I indicates, adhesions and adhesive bands are the most important factors in the causation of obstruction in pregnancy. An analysis of the figures of all 3 tables quoted shows that these were the cause in 24 per cent of cases. It is possible that this figure is not a true reflection of the incidence of adhesions, because these authors would seem to have been especially concerned with so-called obstruction resulting from pregnancy *per se*. The adhesions are usually of postoperative, occasionally of inflammatory, origin—due to a previous peritonitis. Congenital bands are a rarity.

In a review of general surgical cases Deaver and Ross (1915) and Wangensteen (1942) point out that postoperative adhesions most frequently arise following appendicectomy, especially after drainage through a midline incision, or following operation on the female genital organs. The importance of appendicectomy as an aetiological factor is also stressed by Grey-Turner (1906) who found in the follow-up of a series of 2,500 cases of appendicectomy that 0.8 per cent developed acute adhesive obstruction of the small bowel. While the onset of obstructive symptoms may occur months or years after laparotomy, Deaver and Ross (1915) found that the average time for such symptoms to develop was $2\frac{1}{4}$ years. It is not without interest to find that adhesions and adhesive bands form the principal causal factor of obstruction in pregnancy, in view of the frequency with which these factors are associated with tubal occlusion and sterility.

(*b*) *Intermural obstruction*. (i) Acute intussusception. Choffin, Mason and Slemons (1937) collected 20 cases from the literature in which intussusception was the aetiological factor. In Ludwig's series intussusception was responsible for 4 cases (4 per cent); Mikulicz-Radecki's (1926) 3 cases (4 per cent); whilst in Eliason's (1937) series there were none. It can be assumed, therefore, that intussusception is a rare complication of pregnancy. Indeed the possibility of invagination of bowel would appear to be less likely during pregnancy because in rising the uterus tautens and elevates the peritoneum from the posterior abdominal wall, providing thus a force tending to cause fixity of the iliocaecal region. It is well to know that the caecum may rise during pregnancy; yet

TABLE I.
Collected Cases to 1913 (Ludwig).

Aetiology	No. of Cases
Adhesions	28
Volvulus	13
Invagination	4
Pregnancy	10
Hernia	7
Miscellaneous (including tumours, cysts, exudates, etc.)	33
Total	95

TABLE II.
Collected Cases 1913–25 (Mukulicz-Radecki).

Aetiology	No. of Cases
Adhesions	15
Volvulus	34
Invagination	3
Tumour	4
Pregnancy certain	10
Pregnancy uncertain	8
Unknown	6
Total	80

TABLE III.
Collected cases 1925–35 (Eliason and Erb).

Aetiology	No. of Cases
Adhesions	14
Volvulus	11
Tumours and cysts	7
Paralytic (inflammatory)	4
Hernia	2
Pregnancy	28
Total	66

Extracted from tables quoted by Eliason and Erb (1937).

any such elevation is controlled and limited by the peritoneal attachment from below. Indeed, if such were not the case intussusception might be a more frequent occurrence.

(ii) Stricture of the small intestine. As cicatricial contracture of the small intestine is, in the majority of cases, the result of tuberculous ulceration, it is not surprising that we were unable to find any reference to this condition as a complication of pregnancy. The association between abdominal tuberculosis and infertility is well known.

(iii) Crohn's Disease. Malignant stricture. The age at which the maximal incidence of malignant stricture of the bowel occurs is in the 6th and 7th decades. It will be obvious, therefore, that malignant disease as a cause of intestinal obstruction in pregnancy must be rare. In a review of the literature Banner *et al.* (1945) found 62 cases of carcinoma of the bowel associated with pregnancy. Should it occur, however, the affected portion of gut will almost inevitably be found in the large bowel—for malignant stricture of the small intestine is an exceptional finding at laparotomy. We have seen one case of carcinoma of the large bowel complicating pregnancy in a patient aged 30 years. The portion of gut affected was caecum and ascending colon. Treatment was by a one-stage resection and iliotransverse colostomy with satisfactory result. The operation, however, was performed before the onset of acute obstructive symptoms.

(*c*) *Intramural obstruction.* Intramural obstruction may be due to gall stone, faecal impaction or stercolith. The first of these is characteristically a condition affecting old women and consequently unlikely to occur during pregnancy. Similarly, faecal impaction is usually found in elderly patients, and in a country where routine antenatal care is the rule should be a very rare aetiological factor. Stercolith formation, often with a foreign body base, such as a fruit stone, is aggravated by constipation. The possibility, therefore, of a stercolith as a causative agent of obstruction in pregnancy must be borne in mind as a possible, although unlikely, aetiological factor.

Volvulus. Ludwig (1913), Eliason (1937) and Mikulicz-Radecki (1926) have shown that volvulus accounted for more than 25 per cent of their total cases of obstruction in pregnancy. Bailey (1946)

states that this condition is relatively common in Eastern Europe—especially volvulus of the sigmoid, because of a relatively long mesocolon—but is extremely uncommon in this country. In addition to affecting the sigmoid, volvulus of the small intestine or the caecum may occur, the former being favoured by the presence of an adhesion from the convexity of the intestinal loop to the parieties or the pelvic organs, while the latter is also favoured by adhesions following appendicectomy and is especially liable to occur when the right half of the colon is displaced, lax and mobile.

From this brief review of the aetiological factors the importance of postoperative adhesions will be noted. As has been pointed out, these are most likely to occur following operations on the pelvic organs, appendicectomy and drainage of the pelvis through the midline incision. It would seem, therefore, that the gynaecologist can best assist in the prevention of intestinal obstruction in both the pregnant and non-pregnant woman by careful peritonealization of stumps, drainage of the lower abdomen through a stab incision rather than through the midline subumbilical incision, and by refraining from appendicectomy as a routine part of all gynaecological operations!

There is a sharp divergence of opinion regarding the possibility of pregnancy *per se* causing obstruction. Leonard (1917) states that "normal intrauterine pregnancy rarely, if ever, causes acute intestinal obstruction." Wilms and Pinard (quoted by Eliason, 1937) agree that it is the "rarest of conditions". On the other hand the authors we quote, in the accompanying tables, show that pregnancy alone was the aetiological factor in 20 per cent of all the cases—indeed in Eliason's series it was the chief single agent in the production of the complication.

These figures, however, can be misleading for, as Eliason states, it is probable that many cases of obstruction due to the usual aetiological factors, such as adhesions, etc., have not been considered of sufficient interest to report in later years. He suggests that the relative incidence of 10 cases due to pregnancy itself out of 95 cases (Table I) is probably a more accurate figure.

Cases of intestinal obstruction in pregnancy without any obvious aetiological factor are said to have been "proved" at autopsy. In the majority of such cases the obstruction has been found low in the sigmoid colon—where the latter crosses the innominate line. Stoeckel (1929) considers that there may be an atony of the gut produced by some disturbance of the autonomic nervous system and that this may be related to a pre-existing severe pyelitis with marked stasis and dilatation of the ureter. If this theory is correct, it is interesting to find that the site of the obstruction is on the left side, whereas in pyelitis of pregnancy it is the right ureter which undergoes greatest change. Moreover the uterus tends to rotate to the right during pregnancy and in a number of cases the infection of the renal tract is probably secondary to the stasis in the ascending colon. For these reasons one might expect the obstruction to affect the right bowel quadrants, rather than the sigmoid colon. Possibly the more sensitively balanced neuro-muscular mechanism and the solid faecal content of the pelvi-rectal area prove the determining factor.

Mechanical factors such as hydramnios, foetal abnormalities, e.g., hydrocephalus causing a marked increase in the size of the uterus, have been considered by various authors, but discarded because so rarely are pregnancies associated with such abnormalities complicated by intestinal obstruction. However, as Eliason (1937)

points out, in pregnancy the female is more constipated than usual and if, to this manifest lack of tone, other elements are added one can conceive that the pressure of the pregnant uterus may assist in sinister developments.

It appears, then, that intestinal obstruction is less common in the pregnant than it is in the non-pregnant woman of the same age. The lower incidence of the complication is probably due to two factors: firstly, that hernia is relatively uncommon in pregnancy and, secondly, that conditions favourable to the development of obstruction—chiefly post-inflammatory adhesions—are more frequently associated with sterility.

Yet, should pregnancy develop in a patient with peritoneal adhesions, certain mechanical factors tend to precipitate obstruction. These will be discussed later in this paper. Here we would emphasize that intestinal obstruction must always be considered when acute abdominal symptoms develop in pregnancy. Let an abdominal scar on a pregnant woman be a line of evidence denoting potential obstruction.

Case Histories.

Case 1. A recently married pregnant girl aged 16 years was admitted to hospital on July 20th 1947, with severe, intermittent abdominal pain of 13 hours' duration and frequent vomiting for 11 hours. She had an appendicectomy in 1945, performed as an emergency operation through a subumbilical incision and without drainage.

Last normal menstrual period, January 10th, 1947. Expected date of delivery October 17th, 1947. The patient booked at our antenatal clinic on April 9th, 1947. No abnormality was discovered and she was referred to her local clinic for supervision until the later weeks of pregnancy. She was well until she was walking home on the 19th July, at 10.10 p.m., when she developed severe epigastric pain, constant at first, later becoming intermittent. At 11.30 p.m. she experienced nausea and vomited about every half-hour until admission to this hospital 11 hours later. Shortly after the pain commenced, the patient began to hiccough, and to experience frequency of micturition but no dysuria. Foetal movements were present. Following appendicectomy in 1945 the girl made a good recovery and there was no history of pain or distension. She had been mildly constipated during her pregnancy.

Temperature 98°F.; pulse 82, good volume: respirations 20. She was pale and there was puffiness of the lower eyelids; the tongue was clean but dry; the skin moist; breathing normal; heart and lungs normal; blood-pressure, 110/70. There was slight bilateral tenderness on deep palpation of the renal angles. The abdomen had good musculature; there was no distension. The uterine fundus was at the level of a 28 weeks' gestation. The uterus was not tender or hard; the foetal heart was heard. No extrauterine mass was palpable. There was an area of tenderness on deep palpation in the epigastrium extending down to the right iliac fossa. There was no rigidity, hyperaesthesia or rebound tenderness detected.

Vaginal and rectal examination revealed no abnormality. Urine: specific gravity 1020, no albumin, acetone or organisms.

Urinary chloride 2 g. per litre. Haemoglobin 86 per cent.

Progress and Treatment.

July 20th. Condition improved until 6 p.m. when the patient vomited a small quantity of yellow fluid. A litre of 10 per cent glucose saline was given intravenously and followed by 500 ml. of 5 per cent glucose in water, calcium gluconate 10 ml. of 10 per cent solution 4 hourly, and sulphadiazine 1 gram, 6 hourly, administered by the intravenous drop.

July 21st. Condition remained satisfactory; pallor less marked; tongue dry. The patient vomited 3 times during the night (25 ounces) and complained of slight abdominal pain for approximately 15 minutes at 6 a.m. There was no associated nausea. On examination there was some slight epigastric distension. Blood urea 25 mg. per cent. Blood-uric acid 4 mg. per cent. Urine: specific gravity 1025; no albumin; a trace of acetone; no leucine or tyrosine crystals.

6 p.m.—Temperature 99.4°F., pulse 100; blood-pressure 135/80. There was no vomiting; the

abdominal distension had increased; the bowel sounds were high-pitched. A turpentine enema was given with good result.

23rd July, 6 p.m. The patient vomited twice in 12 hours (18 ounces). Epigastric distension increased without pain. A Ryle's tube was inserted and the stomach aspirated half-hourly. A further 1,000 ml. of 5 per cent glucose saline with 50 units of insulin were administered intravenously.

24th July. The patient was restless with frequent hiccoughs. Attempts to insert a Miller-Abbott tube past the duodenum failed and X-rays revealed multiple fluid levels in the small gut.

4.30 p.m. Laparotomy under gas, oxygen and ether using a subumbilical midline incision. A small quantity of straw-coloured, free fluid was found in the peritoneal cavity. The uterus was noted to be the size of a 28 weeks' cyesis. The ileum was seen to be distended and the caecum collapsed. Good exposure was assured by gently holding the uterus over to the left. A firm but vascular adhesive band was noted passing from the caecum about 2 inches above the iliocaecal junction to a loop of ileum. Behind and constricted by this band was a second loop of ileum. The band was divided and the caecal end implanted into the wall of the caecum by a purse-string suture. The constricted ileum proved to be viable. The Miller-Abbott tube was then milked down to third part of the duodenum but shortly afterwards the tube receded back to the pylorus. Finally the abdominal wall was closed in layers.

Postoperative sedation included injections of omnopon together with progesterol mg. x b.d. Prophylactic penicillin 100,000 units 6 hourly, and 1,000 units of heparin were added to each litre of intravenous fluid. The Miller-Abbott tube became partially blocked despite sodium bicarbonate clearance wash-outs, and a Ryle's tube was also inserted. Gastro-duodenal tubes were removed on third day following disappearance of distension and satisfactory enema.

On October 17th she had a normal delivery of a 7 pounds 6 ounces healthy male child. Her puerperium was uneventful.

Case 2. Mrs. E. E., aged 34 years, para 2, was admitted to hospital on September 17th, 1947, with acute colicky abdominal pain of 42 hours' duration.

In 1945 she had a myomectomy and Baldy-Webster uterine suspension.

In 1935 and 1937 she had full-time normal deliveries. Last normal menstrual period, June 26th, 1947. Expected date of delivery, April 3rd, 1948.

While stepping on to a bus at 8 a.m. on September 15th, the patient experienced a sudden stabbing pain in the right lower abdomen. The pain was momentary, unaccompanied by nausea, sickness or faintness, so that she was able to continue her journey and carry out her household duties during the day. At 5 p.m. the same evening, whilst sitting at tea, the pain recurred and lasted for approximately 30 minutes. On this occasion there was nausea but no vomiting. For the next 24 hours she felt well and there was no further pain until 5 p.m. September 16th, when she had a third attack of pain, still confined to the right lower quadrant of the abdomen, which lasted only a few minutes. She paid little attention to this and accompanied her husband to the cinema. At 8 p.m. while watching the film, she was suddenly seized with a very violent recurrence of colicky pain which, on this occasion, radiated from the right lower abdomen to the epigastrium. It was intermittent, each attack lasting approximately 30 seconds, recurring every 10 minutes, and associated with frequent vomiting of small quantities of fluid.

She was admitted to hospital 1 hour later (9 p.m. September 16th). She stated her bowels opened regularly, and that there had been a satisfactory stool 12 hours prior to admission. She did not give a history of rigors or urinary symptoms.

Temperature 97.6°F.; pulse 68, respirations 20. Her appearance was healthy; her facies were anxious but of good colour; the tongue was moist and furred; heart and lungs normal. Blood-pressure 132/90. There was no tenderness in costo-vertebral angles. The abdomen was slightly distended; there was moderate generalized tenderness over the whole abdomen but most marked in the right lower abdomen. Where slight rigidity was detected. The fundus uteri was just palpable above the symphysis pubis.

Vaginal examination revealed an anteverted, mobile uterus enlarged to the size of a 12 weeks' gestation; the cervix was soft and the os closed; a moderate degree of tenderness was detected on bimanual examination through the right fornix; no extrauterine mass was palpated.

Urine: Trace of acetone.

An enema yielded a bulky faecal result.

The case was obviously an acute abdominal emergency and a provisional diagnosis of acute intestinal obstruction complicating pregnancy was made. Laparotomy was performed without delay.

Laparotomy under pentothal, gas, oxygen and ether, using a subumbilical midline incision. A moderate quantity of straw-coloured fluid was aspirated from the peritoneal cavity. Distended coils of ileum presented through the abdominal wound. The uterus was noted to be enlarged to the size of a 12 weeks' gestation. There was considerable distortion of the broad ligament and an absence of the round ligament folds in front. The left Fallopian tube and ovary were densely adherent to the posterior aspect of the uterus with the fimbriae of the tube located to the right of the midline. A coil of ileum was closely incorporated in this tubo-ovarian adhesion and in addition entered depression near the right cornua of the uterus, to which it was so densely adherent for approximately 3 inches that it could only be freed with difficulty by sharp dissection, leaving a cavity which was subsequently closed with catgut. The raw areas of bowel were infolded with continuous atraumatic sutures after the viability of the gut had been established. Adequate patency ensured, the abdomen was closed in layers.

A Ryle's tube was inserted following operation and the gastric contents aspirated 2 hourly by means of a 20 ml. syringe. Fluid and salt balance were maintained by means of an intravenous drip. Omnopon gr. ⅓ was administered by injection 1 hour after operation and repeated in 8 hours. Progesterone mg. x b.d. was given as a prophylactic against possible abortion.

The patient made an uneventful recovery and was discharged from hospital on the 17th day following operation. She attended the antenatal clinic subsequently, when the pregnancy was noted to be continuing undisturbed.

Discussion of Case Records.

It is generally accepted that there is a high maternal mortality associated with intestinal obstruction in pregnancy. Study of 3 tables quoted in part in this paper show that the mortality varied between 21 per cent and 54 per cent, which compared with an over-all mortality-rate of about 30 per cent found with obstruction in the non-pregnant patient. This in great part is a mortality resulting from delay in treatment coupled with the difficulty in operative procedure.

A careful appreciation of dehydration and adequate stabilization of the daily salt-water balance will do much to improve mortality figures. We can lay little stress on the biochemical assessment of dehydration because blood changes are late in appearance and misleading. It is suggested that a common fault is to underestimate the amount of fluid required. Fluid loss amounts to 1,500 ml. per day if water intake is stopped (2 per cent of body weight). Aird (1948) estimates that a non-pregnant patient with obstruction and presenting clinical evidence of dehydration has lost about 6 per cent of body weight and will need therefore at least 8 litres of fluid in the 24 hours following admission (which figure includes 200 ml. per hour to replace intestinal juices, evaporation and urine output and 4.2 litres to replace fluid already lost). Her salt needs—5 g. per day added to about 20 g. of salt which may be presumed as lost before admission—can be supplied as normal saline and the remainder of the fluid given as glucose water. A further 5 g. of salt should be added for every litre of vomited or aspirated gastro-intestinal fluid. The number of litres required multiplied by 12 gives the rate of drip per minute. It is important to note that these figures refer to the replacement of salt and fluid in the dehydrated non-pregnant patient. The quantities required are large and it is probable that less fluid is required to relieve dehydration of a corresponding clinical level in the pregnant patient. It would seem that the pregnant woman presents clinical evidence of dehydration more quickly and with less fluid and electrolyte loss than would be necessary to produce a

similar state in the non-pregnant woman. The duration of pregnancy would be another determining factor.

We would agree with Marriott (1947) that 24 hours is too long a time for periodic reviews of the output, and this is especially true should labour have commenced. Care must be taken lest excessive salt be administered; yet in pregnancy more water can be replaced without the fear that it will not be retained unless covered by additional salt therapy. Excessive salt will increase the strain on already overworked kidneys, especially during pregnancy, when the minimum excretory volume of urine will be raised to cope with extra waste products. In treating dehydration, the Fantus test (for urinary chloride) is of value and has the advantage of being a rapid sideroom test; also useful are serial urinary volume and specific gravity readings. Again we would emphasize that a careful clinical assessment is of paramount value. It is apparent that until we have a more exact appreciation of fluid-electrolyte changes in normal pregnancy, we cannot hope to accurately gauge replacement requirements under pathological conditions.

In case 1 the obstruction resulted from a post-appendicectomy adhesion between a loop of ileum and the caecum. It is suggested that in this type of lesion a mechanical factor tending to precipitate obstruction might be similar to that considered as a cause of intestinal obstruction following an abdomino-perineal resection of the rectum. In this procedure a wide peritoneal resection may result in a traction descent of a loop of ileum. It is possible that the rising uterus may similarly pull down the posterior parietal peritoneum and thereby cause a loop of ileum to be drawn down. Contrariwise other parts of the small intestine may at the same time be pushed upwards in the abdomen.

In case 2 it will be seen that the offending adhesion was related to the posterior surface of the broad ligament and uterus which had been ventrisuspended by the Baldy-Webster technique. No herniation of bowel into a broad ligament fenestra could be detected in this case, such being the well-known occurrence resulting in intestinal obstruction after this operation (Schumann and Beecham, 1939, record two such cases).

It will be noted in case 1 that 3 days elapsed before laparotomy was performed. At operation, however, the patients general condition was satisfactory and this we attribute to adequate fluid and salt replacement therapy. It is known that whilst expectant treatment may prove satisfactory in certain simple obstructions, unsuspected strangulation will be unnecessarily fatal in others. " In some quarters the introduction of suction drainage has given a fall in the fatality rate of occlusion but a rise in that of strangulation, operation in the latter condition being sometimes dangerously delayed by failure to distinguish it from occlusion " (Aird). In addition it seems reasonable to assume that when the metabolic changes which occur in intestinal obstruction are superimposed on the unstable metabolism of the pregnant woman, more particularly salt water and acid base equilibrium, the outlook must be regarded as more serious. We are reminded of two surgical dicta, first that " operation must be prompt but not precipitate " (Wilkie, 1932), and secondly the adage quoted by Vick (1932) that " if you put a patient on the table cold, you will take him off colder."

Abdominal distension may be slow to appear. In case 1 distension was not detected until 36 hours after the initial symptoms. In case 2 distension was only very slightly evident prior to operation. It would appear that despite atonicity of

the bowel in pregnancy, distension may be late in appearing—a feature frequently noted with obstruction in the non-pregnant.

In case 1 it proved impossible to pass the Miller-Abbott tube beyond the pylorus until operation, when it was milked down into the third part of the duodenum. However, prior to closure of the abdomen the tube was noted to have receded to the pylorus and required replacement. Anti-peristalsis may have caused this regression. Further, partial blockage of the tube occurred shortly after operation, necessitating the additional use of a Ryle's tube. Difficulty in the correct positioning of the Miller-Abbott tube has been noted in the non-pregnant state, and we are of the opinion that pregnancy increases this difficulty on account of the enlarged uterus. Moreover, the greater the degree of obstruction, and therefore the greater the need for intubation, the greater is the difficulty in passing the tube. This would appear to be due to a kink resulting from forward displacement of the stomach and duodenum. Therefore in order to ensure that the tube has been correctly positioned, and has not curled up inside the stomach, check radiography for the position of the tip of the tube is more than ever essential. Where difficulty is experienced with the Miller-Abbott tube, a Ryle or Wangensteen tube passed into the stomach will enable the gastric contents to be aspirated. This procedure was adopted in both cases. Certainly vomiting will be relieved and gastric contents prevented from passing to the distended loops below, yet adequate decompression of these loops will not be achieved without the Miller-Abbott or similar intubation. This difficulty in satisfactory decompression in the pregnant woman is yet another argument for early surgical interference. We nevertheless believe an attempt at Miller-Abbott intubation worth while. The passage of such a tube before operation has the advantage that it reduces anaesthetic vomiting and facilitates intra-abdominal manipulation. The dangers of laryngeal oedema, bowel perforation and inability to retract the tube through coiling are rare. While intubation suction is being maintained, it is well to limit fluid by mouth to not more than 120 ml. 4 hourly, lest salt be washed out and the salt balance be further upset.

In both cases care was taken to exclude a renal tract infection which, as we have stated, may very rarely occur as an associated complication.

Diagnosis.

No attempt will be made to discuss diagnosis in detail but only to emphasize certain features.

The 4 cardinal signs of obstruction, vomiting, colic, distension, and absolute constipation may not always be present. The added difficulty is that these signs are frequently associated with a pregnancy uncomplicated by obstruction.

The question will always arise, Is the vomiting obstructive or non-obstructive? In this respect mention will only be made of two adjuncts in diagnosis—radiological and diagnostic enema.

1. *Radiographic diagnosis.* The gas normally present in the colon can generally be evacuated by an enema, so that if the colon remains distended with gas after this has been administered, an obstruction is almost certainly present. The presence of gas and fluid levels in the small intestine is definite evidence of obstruction. Incomplete obstructions are more problematic. For example, in partial obstruction of the ileum, gas may be present in both the colon and ileum. After evacuation of the gas in the colon by an enema, more gas may descend from ileum to replace the removed sample. The disappearance, or otherwise, of gaseous distension noted by serial radio-

graphs provides a useful guide to the success of treatment. Further if, after the colon is emptied of gas, the small intestine remains distended, obstruction of the latter is present.

2. *Enema diagnosis.* If fluid from a half-pint saline or salt and water enema is returned only slightly coloured and unaccompanied by flatus, obstruction can be assumed to be complete. However, results from enemas are frequently difficult to interpret by nurse and later by surgeon, and in recent obstruction a "satisfactory faecal result" may be obtained. The value of comparison radiographs before and after enemas has been mentioned. Strangulation should be suspected if the enema is blood-stained.

The immediate recognition of strangulation is essential. Useful guides are the poor general condition of the patient, the rising pulse (usually little altered in simple obstruction), frequently increasingly severe colicky pain, rebound tenderness, and persistence of pain for longer than 2 hours following adequate gastro-duodenal drainage. Should strangulation be suspected, operation must be immediate. With simple obstruction, pre-operative correction of salt water deficiency is generally advisable.

With many others, we agree that pressure of the pregnant uterus will rarely if ever cause obstruction. It is said that such an obstruction occurs in the recto-sigmoid area, yet we know that obstructive signs are very slow to develop in this area. Moreover, in the experimental animal, simple occlusion at a corresponding site can be maintained for a month or more without symptoms.

It is significant that in the two largest collected case series of intestinal obstruction, 6,892 cases collected by Vick (1932), and 3,064 cases collected by Souttar (1925), reference is made to obstruction in pregnancy. The over-all mortality in Vick's series was 26.2 per cent, and the mortality in obstruction resulting from adhesions 32.9 per cent. This was before the general introduction of suction and saline therapy.

A close examination of the case histories recorded by Eliason and Erb in their paper on intestinal obstruction in pregnancy suggests that at least two of their patients did not have true obstruction; ileus possibly. Thus one often meets with a patient who within a few days following a laparotomy develops symptoms suggestive of organic obstruction, but who almost invariably responds to conservative measures. We have tried to emphasize the importance of deciding whether or not organic obstruction exists in any particular patient. In one of Eliason's cases, vomiting persisted and distension appeared after an appendicectomy performed at the 6th month of pregnancy. Symptoms were relieved by an enema. In a second case signs of obstruction at the 4th month were relieved by an enema given in the knee-chest position, considered by the above writers to have relieved the effect of pressure by the pregnant uterus. In their third case, obstructive signs appeared at 5th month of pregnancy and were relieved by a caecostomy followed by a surgical induction! We note that both these patients gave a history of appendicectomy.

Chronic constipation is so common in pregnancy and may closely simulate acute intestinal obstruction, particularly if impacted faeces become tightly lodged in the colon. In such circumstances an adequate enema will generally give relief and sufficient flatus be passed to prevent serious distension.

Summary.

Two cases of pregnancy complicated by intestinal obstruction are recorded. The obstruction in the first case was the result of a post-appendicectomy adhesion, and

in the second case followed a Baldy-Webster ventrisuspension operation.

The incidence, aetiology, diagnosis and treatment of intestinal obstruction in pregnancy are discussed. Emphasis is placed on the importance of considering intestinal obstruction in evaluating acute abdominal symptoms in pregnancy.

These cases have been published at the instigation and with the help of Professor James Young, Director, and we wish, too, to thank Professor Ian Aird, who advised on the care of Case 1, and who helped us greatly with his advice.

REFERENCES.

Aird, I. (1948): *Companion to Advanced Surgical Studies*. (In Press.)

Bailey, H., and Love, R. J. H. (1946): *Short Practice of Surgery*. H. K. Lewis and Co. London.

Banner, E. A., Hunt, A. A., and Dixon, C. F. (1945): *Surg., Gynaec. Obstet.*, **80**, 211.

Bemmis, G. G. (1932): *Amer. J. Obst. Gynec.*, **24**, 436.

Bonney, V. (1944): *Textbook of Gynaecological Surgery*. Cassell and Co. Ltd.

Choffin, L., Mason, V. R., and Slemons, J. M. (1937): *Surg., Gynaec. Obstet.*, **64**, 111.

Cope, V. Z. (1940): *Early Diagnosis of the Acute Abdomen*. Oxford University Press. London.

Deaver, J. B., and Ross, G. G. (1915): *Ann. Surg.*, **61**, 198.

Eliason, E., and Erb, W. H. (1937): *Surgery*, **1**, 65.

Ludwig (1913): *Z. Geburtsh. Gynäk.*, **75**, 324.

Leonard (1917): *Virginia M. Seminonth*, **22**, 30.

Marriott, H. L. (1947): *Brit. med. J.*, **1**, 328.

Mikulicz-Radecki (1926): *München. Med. Wehnschr.*, **2**, 1352.

Schumann, E. A., Beecham, C. T. (1939): *Pennsylvania med. J.*, **42**, 1032.

Souttar, H. S. (1925): *Brit. med. J.*, **2**, 1000.

Stoeckel (1929): *Zentralb. f. Gynäk.*, **53**, 1462.

Smith, J. A., and Bartlett, M. K. (1940): *New Eng. J. Med.*, **223**, 529.

Titus, P. (1937): *Management of Obstetric Difficulties*. Henry Kimpton, London.

Turner, G. G. (1906): *Brit. med. J.*, **2**, 1696.

Vick, B. M. (1932): *Brit. med. J.*, **2**, 545.

Wangensteen, O. H. (1942): *Intestinal Obstruction*. Charles C. Thomas, Baltimore.

Wilkie, D. P. D. (1932): *Brit. med. J.*, **2**, 545.

A CASE OF INTESTINAL OBSTRUCTION ASSOCIATED WITH A RUPTURED ENTEROCELE

BY

WALTER THOMPSON, M.B., F.R.C.S.,
Surgical Chief Assistant, Manchester Royal Infirmary

A REPORT by Daley and Callum (1946) of "A Case of Intestinal Obstruction Associated with Complete Procidentia" prompts me to report the following case.

History. About 6 p.m. on 4th October, 1947, a lady of 61 years was admitted to the Manchester Royal Infirmary complaining of "something having come down" suddenly 4 hours previously, and of severe lower abdominal pain. Eight years ago she had had a colporrhaphy performed and for the past 6 years "something had been coming down," but she had always been able to replace it.

Examination. A loop of purplish, very swollen, large bowel could be seen protruding from the vulva. Increased peristaltic sounds were present on abdominal auscultation and the patient looked pale and shocked.

Operation. Under low spinal anaesthesia the prolapsed loop of bowel was carefully cleansed with saline and the vulva and vagina washed out with Dettol solution. On exploration of the vagina a loop of bowel was found to be coming through a hole, one inch in diameter, in the posterior fornix. The loop could not be replaced so the posterior vaginal wall was slit downwards in the midline. The loop of bowel now gradually changed colour and there was no sign of necrosis at the constriction ring; the vessels in the mesentery could be felt to be pulsating normally and there was no venous thrombosis. After further cleansing, the viable pelvic colon was returned to the abdominal cavity. The peritoneum was stripped from the vaginal vault and closed separately. The operation was then completed by a normal posterior colporrhaphy and perineorrhaphy. There was no ptosis of the anterior vaginal wall and therefore an anterior colporrhaphy was unnecessary.

Postoperative course. The patient progressed very favourably and the temperature remained normal throughout convalescence: no complications developed. When last seen in February 1948, she stated that she had never felt better.

DISCUSSION.

No cause could be discovered for the sudden rupture of the hernia of the vaginal vault. There is no doubt that there was a localized area of weakness high up in the posterior vaginal wall following the previous colporrhaphy operation. The site of rupture was carefully examined and showed no evidence of recent mechanical trauma or inflammation. It would appear that the rupture had occurred with some normal rise of intra-abdominal pressure, the hernia of the pouch of Douglas having become thinned out at one side. This case was successfully dealt with from below, but at the time of commencing treatment we could not be sure whether the loop of gut was viable; however, after releasing the constriction ring, this problem was settled. Further, the bowel was easily brought down and it would have been possible to perform a resection and end-to-end suture from below. If this had been necessary the operation would, of course, have been completed by an abdominal colostomy.

I would like to thank Mr. A. H. Southam, M.D., F.R.C.S., for allowing me to publish this case.

REFERENCE.

Daley, D., and Callum, E. N. (1946): *J. Obstet. Gynaec.*, **53**, 68.

JAMES HAYWARD WILLETT

Obituary

JAMES HAYWARD WILLETT

M.D., F.R.C.O.G.

JAMES HAYWARD WILLETT died in Tarporley, Cheshire, on July 13th, 1948. He was born on October 20th, 1875, and was educated privately in Chester, and at Victoria University, where he qualified M.B., in 1897. Younger readers may not know that Victoria University was the name given to the combined body formed by Owen's College, Manchester, and the University Colleges of Liverpool and Leeds before each of these became unversities in their own cities. This change had taken place by the time Willett obtained his M.D. (Liverpool) in 1908.

After he had held some house appointments, the South African War had started, and Willett volunteered for service as a medical officer. He was attached to the 1st Dragoon Guards and for his service received the Queen's South African medal with three bars—Orange Free State, Transvaal, Laing's Nek. The excitement of war was for him coloured by romance, for it was during his service in South Africa that he met the lady, Gertrude Ellen Serridge, who became his wife.

When he returned to Liverpool he devoted himself to obstetrics and gynaecology. He was appointed to the staff of the Hospital for Women in 1902 and to that of the Maternity Hospital in 1909. In 1905 he was appointed Demonstrator and Subcurator of the museum in the Department of Obstetrics and Gynaecology in the University of Liverpool under Professor Briggs. At that time Professor Briggs was developing and expanding the museum, and Willett gave a great deal of time and devoted service to mounting, describing and arranging specimens. He remained actively working in the department until 1911.

He was a Foundation Fellow of the Royal College of Obstetricians and Gynaecologists.

Willett was a retiring man of a very quiet disposition. He wrote little, but was an active member of the North of England Obstetrical and Gynaecological Society which he joined in 1901, and of which he was President in 1914, but in this year war again intervened and he never had the opportunity to deliver his presidential address.

As a gynaecologist his diagnostic ability was considerable, but in the years when the writer knew him his operating was handicapped by poor eyesight. As an obstetrician he excelled and he was the master of the various vaginal manipulative manoeuvres. He insisted on an assessment of the weight of the expected child by palpation of the mother's abdomen long before this was accepted practice and was himself so skilled that his own estimates were rarely more than a quarter of a pound out. His name will

always be associated with the foetal scalp forceps he contrived for use in cases of placenta praevia.

He was a capable, painstaking and patient teacher whose students were genuinely fond of him.

Those of us who were privileged to know him will remember him as a very kindly and helpful senior whose excellent obstetrical judgement and skill would have been more widely known had he been of a less shy and sensitive character.

Dr. Willett survived his wife and had no children.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A meeting of the Council was held in the College House, on Saturday, 24th July, 1948, with the President, Sir William Gilliatt, in the Chair.

SIR WILLIAM GILLIATT, *C.V.O.*, M.D., M.S., F.R.C.P., F.R.C.S., was re-elected President.

The following officers were also re-elected:

Vice-Presidents.

SIR WILLIAM FLETCHER SHAW, M.D., M.M.S.A.(Hon.), F.R.C.O.G.

JAMES M. WYATT, F.R.S.C., F.R.C.O.G.

Honorary Treasurer.

ARTHUR A. GEMMELL, M.A., M.D., F.R.C.S.E., F.R.C.O.G.

Honorary Secretary.

HUMPHREY G. E. ARTHURE, M.D., F.R.C.S., M.R.C.O.G.

Honorary Librarian.

FREDERICK W. ROQUES, M.A., M.D., M.Ch., F.R.C.S., F.R.C.O.G.

Honorary Curator of the Museum.

ALECK W. BOURNE, M.B., B.Ch., F.R.C.S., F.R.C.O.G.

The following were admitted to the Fellowship of the College:

Francis Richard William Kinkead Allen.
James Bruce Dewar.
Peter Joseph Kearns.
Hector Joseph MacLennan.
George Randolphe Sparrow.

The following were admitted to the Membership of the College:

Sydney Graham Aitken.
Islay Cecil Barne.
Wallace Barr.
Fred Benjamin.
Arthur Baillie Higginson.

The following candidates were elected to the Membership of the College:

Tariq Munir Abbas.
Ian Struan Robertson Bain.
Henrietta B. Banting.
Trevor Lewys Stanhope Baynes.
Samuel Behrman.
Douglas Charles Aitchinson Bevis.
Charles Christopher Bowley.
Tristam St. Vincent William Buss.
Lloyd Woodrow Cox.
Thomas Elliot Elliot.
Premavathi Maddimsetti Haidu.
Mary Elizabeth Egerton.
Margaret Fitzherbert.
Gilbert McIlwrick Forsyth.
Harold Derek Freeth.
George Barton Gibson.

John Hartley Gibson.
Andrew Graham.
Alfred Henry Grenz.
Constance Amy Grey.
Harold Bickford Hattam.
Carl Clifford Henneberg.
Ebbie Hesselberg.
Dennis Woodfall Higson.
John Colgate Holman.
Kenneth Robert Hudson.
Alun Gareth Jones.
James Barclay Joyce.
Roshan Ardeshir Irani.
William Thomas Kenny.
George Gladstone Kerster.
Robert Arthur Hugh Kinch.
Samuel Lask.
Thomas Loftus Townshend Lewis.
Ethna West Little.
Biohn Lynn Forsyth McConnachie.
William Macfarlane.
John Macdonald McKiddie.
Stephen Herbert Madden.
Helen Margaret Mayer.
Gordon William Heyes Millington.
Frank Lionel Edward Musgrove.
Charles Godfree Nairn.
James Raymond Norris.
John Joseph Francis O'Sullivan.
Joseph Henry Patterson.
Anthony Cecil Pearson.
William Henry Peck.
Stanley Dreland Perchard.
David Prysor-Jones.
Mohammad Siddique Qureshi.
Edward Harford Rees.
Stanley Mckae Reid.
Hujohn Armstrong Ripman.
Donald Norman Struan Robertson.
Helen Margaret Russell.
Basil Walter Sanderson.
Humara Sayeed.
Saran Abdulkadir Siddiki.
George Alfred Silley.
Alan Ambery Smith.
Tom Smith.
George John Sophian.
Christine Margaret Stacey.
Patrick Christopher Steptoe.
Christopher Seymor Newton Swan.
Ralph Arnold Thatcher.
Gwyn Stuart Thomas.
Robert George Whitelaw.
Philip de Silva Wijesekera.
Rhys Meyrick Williams.
Martin Sadler Williamson.
Harold Geoffrey Wolskel.
Peter Spence Wright.
Ratcliffe Bowen Wright.

Preliminary Notice

THE TWELFTH BRITISH CONGRESS OF OBSTETRICS AND GYNAECOLOGY, JULY 1949

To be held in the Friends Meeting House, Euston Road, London.

President: SIR EARDLEY HOLLAND.

Hon. Secretaries: A. JOSEPH WRIGLEY and IAN JACKSON.

58 Queen Anne Street (Royal College of Obstetricians and Gynaecologists), London, W.1.

WEDNESDAY, JULY 6TH.

Morning Session, 10.0 a.m. (*Chairman:* THE PRESIDENT).

The Congress will be declared open by the Minister of Health.

"Modern Caesarean Section."
Introduced by Mr. McIntosh Marshall (Liverpool).

Afternoon Session, 2.0 p.m.

(1) **Guest Paper.** Dr. Joe Meigs (Massachusetts).

(2) **"Pregnanediol."**
Introduced by Prof. C. F. Marrian (Edinburgh) and Dr. G. I. M. Swyer (London).

THURSDAY, JULY 7TH.

Morning Session. 10.0 a.m.

"Essential Hypertension in Pregnancy."
Introduced by Prof. George Pickering (London) and Prof. F. J. Browne (London).

Afternoon Session, 2.0 p.m.

(1) **"Hernia of Pouch of Douglas."**
Introduced by Mr. Charles Read (London).

(2) **"The Management of Pregnancy in Diabetics."**
Introduced by Mr. John Peel (London) and Prof. D. M. Dunlop (Edinburgh).

FRIDAY, JULY 8TH.

Morning Session, 10.0 a.m.

"Diagnosis and Prognosis of Carcinoma of the Uterus."
Introduced by Dr. J. E. Ayre (Montreal) and Dr. Spears (Cambridge).

Afternoon Session, 2.0 p.m.

Discussion on Maternal Mortality.
Introduced by Sir William Gilliatt (London).

Owing to the difficulties that exist at the present time in arranging hotel accommodation, travel, etc., the Hon. Secretaries would like to have the names of those who hope to attend by March 31st, 1949, at the latest, and, if possible, very much before that date.

BRITISH MEDICAL ASSOCIATION

THE KATHERINE BISHOP HARMAN PRIZE
for the encouragement of Research into the Disorders Incident to Maternity

The Council of the British Medical Association is prepared to consider an award of the KATHERINE BISHOP HARMAN PRIZE in the year 1949. The value of the Prize is £75.

The purpose of the Prize, founded in 1926, is the encouragement of study and research directed to the diminution and avoidance of the risks to health and life that are apt to arise in pregnancy and child-bearing. It will be awarded for the best Essay submitted in open competition, competitors being left free to select the work they wish to present, provided this falls within the scope of the Prize.

Any medical practitioner registered in the British Empire is eligible to compete.

Should the Council of the Association decide that no Essay submitted is of sufficient merit, the Prize will not be awarded in 1949, but will be offered again in the year next following this decision, and in this event the money value of the Prize on the occasion in question shall be such proportion of the accumulated income as the Council shall determine. The decision of the Council will be final.

Each Essay must be typewritten or printed in the English language, must be distinguished by a motto, and must be accompanied by a sealed envelope marked with the same motto and enclosing the candidate's name and address.

Essays must be forwarded so as to reach the Secretary, British Medical Association House, Tavistock Square, London, W.C.1, not later than 31st December, 1948.

Inquiries relative to the Prize should be addressed to the Secretary.

CHARLES HILL,
Secretary.

British Medical Association House,
Tavistock Square, London, W.C.1.
April 1948.

BOOK REVIEWS

"Operative Gynaecology." By H. S. CROSSEN, M.D., and R. J. CROSSEN, M.D. Sixth edition. London: Henry Kimpton, 1948. Price 75s. net.

IN 1915 H. S. Crossen stated the objective of his first edition to be the selection of treatment best suited to a particular patient by an operator, familiar with the pathology of the pelvis and with the various operative procedures available, after careful study of the individual case. In this sixth edition the authors reaffirm that selective treatment is their aim.

The details of operative technique and clinical management of patients before and after operation are thoroughly and clearly described and well illustrated. There are special chapters devoted to the Urinary Tract, the Intestinal Tract, and to Nervous and Mental Symptoms in Gynaecological Surgery. In this country the name of McIndoe will be missed from the account of treatment for Absence of the Vagina, and the name of Millin from the section on Defective Urinary Control. The radical abdominal operation for cancer of the cervix appears under the heading "Operations of Historical Importance", perhaps the sections on Vaginal Hysterectomy for Radium Implantation, Abdominal operation for Radium Implantation and Needle Treatment of Parametrium (Interstitial Radiation) would be more appropriately so described.

In the chapter on Myoma of the Uterus, an interesting section describes the experience of the authors in radiation therapy of uterine myoma, with a discussion of indications, limitations, and critical analysis of results, the typical case being a patient of climacteric age with a medium size myomatous uterus, bleeding as a principal symptom, and the pelvis otherwise clear. In regard to the influence of myoma radiation on the incidence of subsequent uterine and ovarian malignancy a decided reduction is claimed; each type of malignancy was more than twice as frequent in the non-radiated cases as in those given radiation therapy.

Chief emphasis in this edition is on the prevention of cancer. For chronic cervicitis, with or without suspicion of early malignancy, conical excision by the electric cutting wire is recommended in preference to cauterization or coagulation, so that microscopic examination of all tissue removed may be made. For delayed menopause and erratic menopausal bleeding the possibility of endometrial malignancy calls for careful examination: if no local disease is found, radium treatment to suppress the ovarian and endometrial activity is recommended. There is a lengthy discussion of the menace of "silent" ovarian carcinoma, where insidious spread of the disease beyond hope of cure so often precedes the onset of warning symptoms. The sections dealing with leucoplakic vulvitis and cancer of the vulva based on the work of Taussig are excellent, the descriptions of the lymphatics of the external genitals being from Sappey, from Poirer, and from Cunéo and Marcille.

There are many warnings, and references to several critical analyses of postoperative deaths. The book is well printed, convenient to handle, amply illustrated, pleasant to read, and throughout reflects long experience and mature judgement.

"Textbook for Midwives." By WILFRED SHAW, M.A., M.D., F.R.C.S., F.R.C.O.G. 689 pages, 223 illustrations. London: J. and A. Churchill, Ltd.

THE author decided to write this book after experience of teaching pupil midwives during the war. He holds the view that "a midwife performs one of the most vital duties in modern society, and that her importance is neither realized nor sufficiently recognized." He is convinced that "the status of

midwives will be improved far beyond what it is at present, and that ultimately midwives will hold a position intermediate between that of a trained nurse and a general practitioner." Because of these beliefs, the author has attempted to incorporate in the book details and descriptions of importance to a student on the level of the Sister Tutor. A glossary has been introduced to explain unfamiliar terms.

Mr. Shaw has succeeded admirably in his task. There is little doubt that this book will become the standard textbook for those reading for the Teacher's Diploma, and a book of reference for the pupil midwife. The medical student may consult with benefit such chapters as those on "the composition of the body fluids", "the cellular structure of the body", and "reproduction".

It is good to see manual removal of the placenta advocated for the midwife in the treatment of continuous postpartum haemorrhage when simpler methods have failed and medical aid is not to hand. But why the aversion to ergometrine?

In the closing chapter of the book there is much food for thought for both midwife and doctor about their relationship and several responsibilities, and no better time than the present could have been chosen to discuss these. Not only is the harmony of the midwife-doctor relationship important but the heavy responsibility of State to each is paramount.

G. GORDON LENNON

REPORTS OF SOCIETIES

EDINBURGH OBSTETRICAL SOCIETY

At a meeting of the Edinburgh Obstetrical Society on 19th May, 1948, the President, Dr. W. F. T. Haultain, in the Chair, a paper was presented by Mr. Charles Read entitled THE ROLE OF SURGERY IN THE TREATMENT OF CARCINOMA OF THE CERVIX.

Mr. Read said that division of opinion centred around the relative merits of radiation and radical surgery in Stage I and Stage II cases. There was little debate in respect of Stage III and Stage IV cases, which were generally unsuitable for surgery. While in many clinics the Wertheim operation had been abandoned when radiotherapy had been generally established, at the Chelsea Hospital for Women this operation had been performed continuously since Mr. Bonney introduced it in 1907, although it had been the practice latterly rather carefully to select the cases. From the published statistics, even the surgical enthusiast must admit that the results of radiotherapy compared favourably with those of surgery; but the question might well be raised whether any of the fatalities after radiotherapy might be avoided by judicious surgical procedures. Mr. Read suggested that there were 7 indications for a surgical attack upon cervical carcinoma, namely

(1) Radio-resistant growths proved either clinically or cytologically.
(2) Columnar celled carcinoma of the cervix.
(3) Vaginal vault stenosis.
(4) The presence of large fibroids or ovarian cysts complicating the growth.
(5) Salpingitis with cervical cancer.
(6) Refusal of radiation by the patient.
(7) Pregnancy complicating cervical carcinoma.

After discussing each of these indications separately, Mr. Read dealt with the Wertheim operation after previous irradiation. Although this did increase technical difficulties, the operation in proved radio-resistant cases was justifiable, experience in the Chelsea Hospital showing a 5-year survival rate of 44.4 per cent in 34 Stage I and 20 Stage II growths.

Regarding iliac lymphadenectomy, from material obtained at the Wertheim operation, from autopsy material, and from that obtained at the operation of lymphadenectomy without removal of the uterus, Mr. Read had come to the conclusion that the rate of gland involvement was approximately

Stage I—20–25 per cent
Stage II—30–35 per cent
Stage III—40–50 per cent
Stage IV—Over 60 per cent

From these it would appear that treatment by radium alone, using vaginal applicators only, could never hope to give adequate radiation to the lymphatic field. It therefore seemed that there was a place for iliac lymphadenectomy in Stage III cases which had been cured locally by radium, and that such a procedure could well be extended to include Stage II cases and selected cases of Stage I growth.

Mr. Read discussed the technique of the Wertheim operation with particular reference to the carrying out of lymphadenectomy early in the operation, leaving the iliac and obturator lymph node chain attached to the uterus throughout, to the need to remove at least the upper half of the vagina, and to the use of plasma or blood transfusion. He recorded an incidence of postoperative urinary fistulae of 3.1 per cent.

In discussion Professor Robert McWhirter said he found comparatively few points of divergence of opinion between Mr. Read and himself. At one time there had been sharp differences between surgeons and radiologists, but increasing experience had narrowed the area of disagreement very considerably, and further study might yet obliterate it. His own opinions were governed not only by technical matters of detail but also by certain general principles of approach. Of these he placed first the need to consider each case of cancer individually, and to treat the patient and not the tumour. The prime object should be to make her

more comfortable and any treatment which cured the cancer without achieving this end was a failure.

The maximum distance from the cervical canal at which radium might be expected to be effective was 3 cm. Growths which extended beyond that distance were insusceptible to radium. The tumour lethal dose varied in different tumours and some might justifiably be described as radio-resistant, but the most important limiting factor in regard to treatment was the restricted striking distance of radium. Radio-sensitivity of tumours was a variable factor. At the moment the opinion of the histologist was of limited value in its recognition, and a new approach to its histological study was necessary. Possibly the observation of the irradiation effects in successive biopsies might prove a valuable field of investigation. It was difficult to envisage any great increase in radium range in the near future, apart possibly from improved applicators, with more efficient screening of the bladder and rectum. It was the need to avoid damage to these organs which chiefly restricted the dosage.

When supplementing the radium treatment with X-rays was first attempted, the whole pelvis was irradiated; and not uncommonly necrosis developed in tissues which had already received a high dosage from radium. It became obvious that if X-ray treatment was to be really beneficial, it must be closely aligned to the radium treatment. Patients with cells just outside the effective range of radium were far more likely to benefit from X-rays than patients with cells far out in the pelvis, for these latter advanced cases frequently had distant metastases as well. In order to try to align the 2 methods of treatment, the X-ray fields were planned from the radiographs showing the position of the radium in the uterus, but when vaginal packing was introduced the uterus might be greatly displaced to one or other side of the pelvis and might be displaced upward to a considerable extent. These difficulties could to some extent be overcome by the use of special radium applicators, such as those devised by Richards of Toronto. X-ray therapy alone would remain an unsuitable method of treatment until much more powerful apparatus became available.

Professor McWhirter believed that surgery was the most effective method of treating cancer when it was early and localized. Unfortunately, by the time patients sought advice, the disease was often no longer suitable for treatment by surgery. In criticism of some of the claims for surgical treatment, it must be pointed out that a number of factors operated to produce a favourable selection of cases. For example, the patients submitted to surgery were usually in good condition, not unduly obese and not too old, and restricted to Stage I and early Stage II cases. Because extensive lymphadenectomy must always remain a piecemeal dissection, he thought it unlikely that this practice would greatly improve the eventual prognosis.

He did not believe that an inoperable case could ever be rendered operable by preliminary irradiation, although he believed improvement might be obtained by means of postoperative irradiation with very high voltage X-ray apparatus, and preoperative irradiation in operable cases might be of benefit.

In a review made some time ago, the 5-year survival rate in Edinburgh was 29 per cent of all cases referred. In the most recently analysed cases, the 5-year survival rate was 34 per cent. In the calculation of these survival rates, no case was omitted from the total for any reason whatsoever. He believed that these figures might be improved by the use of surgery where the disease was early and where the tumour was shown to be radio-resistant, and he thought a serious attempt should be made by histologists to recognize resistant tumours, so that the appropriate treatment might be given initially.

The paper was discussed further by Dr. Douglas Miller, Dr. E. C. Fahmy, Dr. Clifford Kennedy, Dr. J. C. Clark, Professor Margaret Fairlie, Dr. R. de Soldenhoff and Professor R. J. Kellar. The President summed up.

REVIEW OF CURRENT LITERATURE

The Journal is fortunate in being able to run this Review in conjunction with the Abstracting Service of the British Medical Association. All the abstracts of this service which cover obstetrical and gynaecological literature and literature on the new-born are at our disposal. The Review will, however, contain in addition abstracts and titles of articles which, though not of sufficient general interest for publication in the monthly volumes published by the British Medical Association, are yet sufficiently important for a specialist journal. It is to be hoped that our readers will collaborate in the preparation of these abstracts. Those who are willing to take part in the service are invited to communicate with the Editor, The Abstracting Service, B.M.A. House, Tavistock Square, London, W.C.1. There is special need of abstracters in foreign languages, and when offering his or her services the writer should indicate the language (apart from English) in which he or she is proficient. The name of the abstracter will be acknowledged in the text and payment will be made at the rate of ten shillings per abstract for English articles and twelve shillings and sixpence per abstract for articles from foreign languages.

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ANATOMY

1412. **Pelvic Mensuration: A Study in the Perpetuation of Error.**
By N. J. EASTMAN. *Obstet. gynec. Surv.*, **3**, 301–329, June 1948. 19 figs., 20 refs.

1413. **Roentgen Pelvimetry.**
By E. G. REUTER. *Texas J. Med.*, **43**, 762–764, Apr. 1948. 1 fig.

1414. **Clinical Interpretation of X-ray Pelvimetry.**
By H. P. TAYLOR. *Ohio St. med. J.*, **44**, 608–611, June 1948. 7 refs.

1415. **A New Technique for Radiopelvimetry (Magnin's Apparatus).** (Un nouveau procédé de radiopelvimétrie (Appareil de Magnin).)
By E. P. NAUDIN. *J. Radiol. Electrol*, **29**, 254–256, 1948. 5 figs.

1416. **Histological Data on the Changes in the Endometrial Vessels of Hypertensive Women.** (Documents histologiques sur les modifications des vaisseaux de l'endomètre de femmes hypertendues.)
By J. BRET and B. DUPERRAT. *Gynéc. et Obstét.*, **47**, 349–358, 1948. 8 figs.

1417. **The Detailed Anatomy of the Paraurethral Ducts in the Adult Human Female.**
By J. W. HUFFMAN. *Amer. J. Obstet. Gynec.*, **55**, 86–101, Jan. 1948. 10 figs., 31 refs.

The detailed anatomy of the paraurethral ducts and glands in the human female is a controversial subject. After reviewing the literature of the subject briefly but comprehensively the author describes his own findings in several adult human female subjects.

His method of study was by wax-model reconstructions. His material was obtained from 11 necropsies. From each a mass of tissue was excised. This contained the entire urethra and the surrounding structures lying beneath the pubic arch, the lower portion of the bladder, and the anterior vaginal wall. After fixation each mass was cut to a size suitable for histological preparation. When so trimmed, each block consisted of the urethra, the periurethral tissues, and the intact suburethral vaginal mucosa. These blocks were then cut transversely into several serial blocks, and subsequently each block was serially sectioned at 10 micra. Every twenty-fifth section was stained with haematoxylin and eosin. When wax models were to be made these sections were placed under a projecting microscope and enlarged. The enlarged images were transferred on to paper; the outlines of the desired structures were traced, and they were transferred from the paper on to wax plates whose thickness was such as to maintain correct longitudinal proportions. The serial waxed plates were subsequently annealed to form models.

The most striking feature of this study is the great extent of the tubules and epithelial-lined pockets which lie about the adult human female urethra. It is popularly considered that this homologue of the prostate is at best a scattering of insignificant tubules or evaginations of the urethra with 2 or occasionally 3 major ducts opening at the urethral orifice and extending laterally and dorsally in the urethral walls. Instead, the prostatic homologue is found most often to be a widespread branching of ductal channels and glands surrounding the female urethra to some extent on all sides, but mostly laterally and posteriorly. The smallest number of ducts found in any specimen was 6 and the largest 31. The glands are branched tubular glands with straight or slightly curved branches which empty into the ducts which in turn open mainly into the distal third of the urethra. The glands are lined with columnar epithelium, which has some secretory activity. The part which the paraurethral ducts may play in the aetiology of lesions of the urethra and anterior vaginal wall is discussed. *Anthony W. Purdie*

1418. **Study of Ureteral Blood Supply and its Bearing on Necrosis of the Ureter Following the Wertheim Operation.**
By J. P. MICHAELS. *Surg. Gynec. Obstet.*, **86** 36–44, Jan. 1948. 2 figs., 55 refs.

The reasons for the gradual return to radical surgery for the treatment of carcinoma of the cervix are outlined—unsatisfactory results of irradiation alone, improved surgical and anaesthetic technique, greater use of blood transfusion, and the advent of chemotherapy. Ureteric fistula is, in the opinion of the author, a major risk associated with the radical surgical technique. Fistulae result from division or crushing of the ureter at the time of operation and also from necrosis due to damage to the blood supply. This damage may involve the periureteric vascular plexus or the main arteries supplying it. To study the blood supply of the ureter the author perfused and injected 8 recently stillborn foetuses with coloured synthetic liquid latex. He found that the chief vessels are "long" arteries arising from one or more of the following vessels: the abdominal aorta adjacent to its bifurcation, the common iliac artery, and the hypogastric artery. These long arteries on reaching the ureter divide into ascending and descending branches, which supply the periureteric plexus and anastomose with vessels from the renal, ovarian, uterine, and vaginal vessels. The smaller vessels arising from these main ones ramify over the surface of the ureter and send branches which pierce its muscular wall. Damage to the blood supply may follow: (1) injury to the long arteries; (2) the formation of exudates and haematomas; (3) vasospasm. This latter may be avoided by resection of the hypogastric plexus during the operation.
J. Stallworthy

PHYSIOLOGY

1419. **The Physiological and Pathological Functions of the Ovaries.** (O prawidlowej i patologicznej czynności jajnika.)

By H. GROMADZKI. *Przeg. Lek.*, 3, 791–799, Dec. 1947. 24 refs.

1420. **The Influence of Thyroid Activity on the Function of the Ovaries.** (Z badan nad wplywem hormonów tarczycy na czynność jajników.)

By W. PAWIK. *Przeg. Lek.*, 4, 23–24, Jan. 1948.

The author discusses, in the light of various recent clinical and experimental investigations, the relation between the thyroid gland and the ovary. His own experiments were made in order to find out what changes are caused in the function of the ovary in white mice by lack of thyroxine. Injections of an aqueous solution of methylthiouracil were used to stop the production of thyroxine. The mice were divided into 6 groups according to the daily dosage of methylthiouracil, which varied from 0.0005 g. to 0.05 g. The oestrus cycles were investigated by means of vaginal smears. Prolongation of dioestrus was observed after 3 to 4 cycles and in some of the animals oestrus was also prolonged. Oestrus ceased entirely 40 to 50 days after the start of the injections. Biopsy of the ovaries of those mice which had been injected for 90 to 150 days revealed congestion, ecchymoses, and the presence of many atretic follicles but no mature follicles. After 90 to 120 days of these injections some of the mice were divided into 2 groups; in one the injections of methylthiouracil were continued, in the other they were stopped. Both groups were put with males of the species. After 6 weeks the mice which had not received injections became pregnant at varying times. The pregnancy and the subsequent litter were normal. The other group remained sterile. The author compares the result of his own experiments with the investigations carried out by others. Insufficient production of gonadotrophin, when the production of thyroxine is stopped, is generally supposed to be the cause of the changes in the ovaries. *C. Uhma*

1421. **The Vaginal Cycle of Elderly Women as a Biological Test of Functional Activity of an Oestrogenic Hormone.** [In Russian.]

By I. D. ARIST. *Akush. Ginek.*, No. 2, 7–9, 1948.

1422. **Estrogens in Urine and Cytology of Vaginal Smears after the use of an Estrogenic Cream.**

By J. EIDELSBERG. *Amer. J. med. Sci.*, 214, 630–632, Dec. 1947. 6 refs.

The fluctuations in estrogen excretion in 4 untreated controls and in 14 patients, before and during the use of an estrogen cream by facial inunction were similar in pattern and not significantly different in amount. Likewise, their vaginal smears appeared to show no significant alteration in cytological cycles. Therefore, in the amounts and by the method applied (3,750 i.u. per week, or +535 i.u. daily) the estrogen cream does not appear to produce any systemic effect.—[Author's summary.]

1423. **The Excretion of Sex Hormones after Hysterectomy.**

By M. L. TSYRULNIKOV. *Akush. Ginek.*, No. 5, 40–46, 1947.

An investigation into the ovarian function of 51 women who had undergone hysterectomy was carried out by estimating urinary excretion of oestrogens and gonadotrophic hormones—18 (35.3 per cent) were found to excrete both oestrogens and gonadotrophic hormone; 5 (9.8 per cent) were found to excrete only oestrogens; 23 (45.1 per cent) were found to excrete only gonadotrophic hormones; and 5 (9.8 per cent) were found to excrete no hormones at all. The author considers that excretion of both oestrogens and gonadotrophic hormones indicates normal activity of the ovaries, while excretion of only oestrogens indicates the beginning of failure of ovarian function, and excretion of gonadotrophic hormone alone or of no hormones at all indicates cessation of ovarian activity (and in the last type cessation of pituitary activity as well). A careful analysis of the cases shows that excretion of the hormones depends on the age at the time of the hysterectomy, on the type of hysterectomy carried out, on the amount of ovarian tissue left, and on the time elapsed since hysterectomy. Ovarian activity persisted in 47.4 per cent of cases when hysterectomy was performed before the age of 35, but in only 28.1 per cent of cases when hysterectomy was performed after the age of 35. Subtotal hysterectomy seems to be the optimum operative procedure, and the removal of one ovary appears to influence adversely the persistence of ovarian function. In 60 per cent of cases ovarian function was still present up to 3 years after the operation; beyond the period of 3 years, ovarian function was present in 22.7 per cent of women who were under 35 at the time of hysterectomy, but in only 9.1 per cent of women who were over 35 at the time of hysterectomy. Menopausal symptoms after hysterectomy did not entirely coincide with absence of excretion of the sex hormones.

Nicolas Tereshchenko

1424. **Muscular Activity of the Fallopian Tube in Different Phases of the Menstrual Cycle, in Pregnancy, and at the Menopause.**

By A. I. ROZHDESTVENSKAYA-OSYAKINA. *Akush. Ginek.*, No. 5, 31–36, 1947.

Four types of experiment were carried out on 140 human Fallopian tubes removed at operation: (1) Observation of spontaneous contractions of the Fallopian tube and its reaction to stimulation (100 experiments). (2) Observation of the flow of coloured water under pressure through the Fallopian tube in the direction from ampulla to uterus and

in the opposite direction (87 experiments). (3) Kymographic recording of the contractions of whole Fallopian tube and of segments of Fallopian tube (203 experiments). (4) Observation of the movement of foreign bodies (actually poppy seeds) introduced into the ampullary end of Fallopian tubes, and recording of the resulting muscular activity (30 experiments). Five series of subjects were chosen: (*a*) Fallopian tubes of women in the first half of a menstrual cycle (15 cases); (*b*) Fallopian tubes of women in the second half of a menstrual cycle (20 cases); (*c*) Fallopian tubes of women in the menopause (6 cases); (*d*) Fallopian tubes of women during normal pregnancies (26 cases); (*e*) Fallopian tubes of women with tubal pregnancies (11 cases). In all cases the muscular activity of the ampullary part of the Fallopian tube was found to be the same, and resembled the pendulum-movement type of activity seen in small intestine. The muscular activity of the other parts of the Fallopian tube was found to vary with its physiological state, and can be classified into 3 types: (1) Very irritable tube, responding readily to slightest stimulation, contractions spasmodic, no peristalsis, no rhythmical or periodic contractions, foreign body tightly gripped but not passed along lumen. Water flows as a thin continuous stream at a pressure of 20 to 25 cm. except during spasmodic contractions, when the flow stops and may not restart for 1 to 2 hours unless the pressure is raised by 5 to 8 cm.; this type of muscular activity occurs during the first half of the menstrual cycle. (2) Tube not irritable and not responding readily to stimuli, contractions peristaltic and rhythmical periodic shortening, foreign body passed along lumen towards uterus. Water flows in intermittent jets at a pressure of 6 to 12 cm.; this type of muscular activity occurs during the second half of the menstrual cycle and during pregnancy. (3) Tube not irritable, not responding to stimulation, no contractions, foreign body evoking no response and remaining stationary. Water flows as it would through a rubber tube of the same diameter; this type of muscular activity occurs after the menopause. The author concludes that the hormonal influences during the first half of the menstrual cycle help to place the Fallopian tube in a position and state favourable for the reception and retention of the maturing ovum, while during the second half of the menstrual cycle and in pregnancy rhythmical muscular activity with lowered tone and excitability occur and thus favour fertilization, implantation, and gestation. Thus a change in the relative proportions of folliculin and lutein may be a factor in the causation of ectopic gestation and sterility. *Nicolas Tereshchenko*

1425. **Physiology of Menstruation.** (Fisiología de la menstruación.)

By J. B. LLUSIA. *Toko-ginec. Práct.*, **7**, 181–254, May 1948. 14 figs.

1426. **Influence of Menstruation on the General Health.** (Beeinflussung des Allgemeinbefindens durch die Uterusfunktion (Menstruation).)

By H. KUSTNER. *Zbl. Gynäk.*, **69**, 1085–1087, 1947.

1427. **Morphological Basis for Menstrual Bleeding. Relation of Regression to the Initiation of Bleeding.**

By J. E. MARKEE. *Bull. N.Y. Acad. Med.*, **24**, 253–268, Apr. 1948. 8 figs., 14 refs.

1428. **Methods of Determining the Time of Ovulation.**

By E. M. JACOBS. *J. Bowman Gray Sch. Med.*, **6**, 56–61, Apr. 1948. 30 refs.

1429. **Adaptation of the Spiral Artery in the Rabbit Ovary to Changes in Organ-size After Stimulation by Gonadotrophins: Effect of Ovulation and Luteinization.**

By S. R. M. REYNOLDS. *Endocrinology*, **40**, 381–387, June 1947. 9 figs., 6 refs.

The arterial supply of the rabbit ovary was visualized by injecting vinylite plastic and digesting the tissue away. The two spiral arteries in the normal rabbit ovary have already been described by Reynolds (*Amer. J. Obstet. Gynec.*, 1947, **53**, 221). When gonadotrophin injections produced ovulation and luteinization there was a "paying-out" of the coils so that the arteries were lengthened and appeared sinuous instead of spiral. Coils became flattened and oblique instead of perpendicular to the ovarian surface. These changes were present for the first 3 days after the injection and the normal state was restored after 6 to 9 days.

[The findings indicate the use of the spiral arrangement in allowing the blood supply to keep pace with rapid increases in tissue volume.]

Peter C. Williams

1430. **Relation between Time of Fertilization and Follicle Cell Dispersal in Rat Ova.**

By S. L. LEONARD, P. L. PERLMAN, and R. KURZROK. *Proc. Soc. exp. Biol., N.Y.*, **66**, 517–518, Dec. 1947. 5 refs.

Since the discovery that the enzyme hyaluronidase from sperm disperses the follicle cells of recently ovulated mammalian ova, a concept has arisen that the action of this enzyme facilitates fertilization by denuding the ova before, or simultaneously with, sperm entry. Complete cell dispersal may be seen when mammalian ova are denuded by hyaluronidase *in vitro*, but observations reported in the present paper indicate no mass removal of follicle cells before fertilization and that sperm penetration precedes the gross denudation of the ovum in the rat. Fertilized ova were recovered from the oviducts of rats in this experiment and examined microscopically before and after hyaluronidase was introduced into each horn of the uterus of a rat in oestrus, the horns being ligated near the cervix to prevent leakage; ova were

recovered 18 to 24 hours later. The results indicate that sperm make their way between the follicle cells and fertilize the ovum before any visible dispersal of follicle cells occurs. Somewhat later the follicle cells are dispersed, freeing the ova. Most of the sperm and hyaluronidase remain in the uterus after copulation, and mass movement of the enzyme from the uterus into the tubes does not seem to play a part in the process of denudation and fertilization. The authors consider that hyaluronidase is produced by those sperm which gain access to the tubes, and that, with the aid of this enzyme, the sperm traverse the follicle cell mass to fertilize the ovum. The later concentration of enzyme is sufficient to denude the ova; this was observed 24 hours after coitus. *Doreen Daley*

1431. **An Improved Method of Extraction and Purification of Relaxin from Fresh Whole Ovaries of the Sow.**

By A. ALBERT, W. L. MONEY, and M. X. ZARROW. *Endocrinology*, **40**, 370–374, June 1947. 4 refs.

Dilute hydrochloric acid (2 per cent) extracts 200 to 300 times more relaxin from fresh ovaries of the sow than had previously been extracted from separated corpora lutea. Relaxin activity was present equally in the corpora lutea and the rest of the ovarian tissue, but not in the follicular fluid. The higher yields are attributed to the fact that ovaries from pregnant sows were used; when such ovaries were extracted they yielded 3,200 to 9,600 units per g., while only 3 to 10 units per g. were obtained from the ovaries of non-pregnant sows. [This big difference affords evidence that relaxin plays some part in pregnancy in animals in which no relaxation of pelvic ligaments takes place at parturition.] A purification process based on acid extraction, absorption on " bentonite ", and isoelectric precipitation is described. It yielded a final product containing 300 units per mg., which is about 10 times purer than the purest previous extract. *Peter C. Williams*

1432. **A Rapid Method for the Estimation of Pregnanediol.**

By J. RABINOVITCH. *Nature, Lond.*, **161**, 605, Apr. 17, 1948.

1433. **Metabolism of Synthetic Oestrogens in Man.**

By A. E. WILDER SMITH. *Nature, Lond.*, **160**, 787, Dec. 6, 1947. 4 refs.

Over-dosage with synthetic oestrogens may alter the path of their excretion by allowing unchanged phenol to be excreted. Thus the metabolism of stilboestrol cannot be conveniently studied by determinations of ethereal sulphate or glucuronic acid. To control experiments on man and animals chemical separation methods checked by bio-assay have been devised (Sahasrabudhe and Wilder Smith, *Biochem. J.*, 1947, **41**, 190). Early results show that less than 1 per cent oestrogen is excreted in the free form. *Magnus Haines*

PREGNANCY

1434. **Temperature Measurements in Mother and Foetus.** (Temperaturmessungen bei Mutter und Frucht.)

By W. BICKENBACH and B. ROEVER. *Zbl. Gynäk.*, **69**, 151–159, 1947. 7 refs.

These authors, with the aid of specially constructed temperature-recording apparatus, measured the temperature in the abdominal cavity, in the uterine muscle, in the uterine cavity, and in the mouth and/or anus of the foetus while it was still in the uterine cavity. These measurements showed that the foetal temperature was on an average 0.7°C. higher than that of the uterine cavity and this was on an average 0.3°C. higher than that of the uterine muscle. The temperature of the uterine muscle was the same as the rectal temperature before the start of an abdominal operation. The rectal temperature during an abdominal operation fell in the course of 45 to 55 minutes by about 0.4°C., but there was no alteration in temperature of the uterine muscle during the whole operation. *Gladys Dodds*

1435. **The Primigravida over 40.** (Die erste Geburt im 5.Lebensdezennium.)

By P. SALACZ. *Zbl. Gynäk.*, **69**, 988–995, 1947. 16 refs.

1436. **Weight Changes in Pregnancy.**

By C. L. SPURLING. *J. Bowman Gray Sch. Med.*, **6**, 65–69, Apr. 1948. 19 refs.

1437. **Studies of Haematology in Pregnancy. I. The Bone Marrow in Normal Pregnancy.** (Estudios sobre hematología de la gestación. I. La medula ósea en la gestación normal.)

By M. MONTOYA GOMEZ. *Clin. y Lab.*, **44**, 170–177, Sept. 1947. 9 figs., 11 refs.

The sternal bone marrow in 150 cases of normal pregnancy and in 50 cases of toxaemia and infection following abortion has been studied. The cases of normal pregnancy were divided into 4 groups: (1) and (2) those in the first and second trimesters; (3) those in the seventh and eighth months which, because of special features of the reaction in late pregnancy, were grouped together and separated from (4) those in the ninth month. Of 400 cells counted, 20.1 per cent belonged to the red-cell series in the first trimester, 21.65 per cent in the second trimester, 25.8 per cent in the seventh and eighth months, and 25.05 per cent in the ninth month. These figures are compared with the level of 18 per cent found in normal individuals by Rohr.

In 75 to 80 per cent of cases the perforation of the bone and aspiration of medulla were unusually easy, as a result of the softening of the bone by increased medullary function, while in 10 per cent there was increased resistance. The erythroblastic reaction is definite in the first trimester, when collections of normoblasts not usually found in non-preg-

nant patients can be seen. In the second trimester collections of reticulated plasma cells have often been observed when there is an erythroblastic reaction, a finding which does not seem to have been noted by other authors. The erythroblastic reaction is most marked in the seventh and eighth months, in spite of a fall in the number of circulating red cells. A normoblastic type of reaction has always been found, and in no case have megaloblasts been seen. The author does not believe that megaloblasts and normoblasts can be produced together, and considers that the megaloblasts reported by Daniachij were really pro-erythroblasts. *Bryan Williams*

1438. **The Main Factors in Erythrocyte Sedimentation during Pregnancy and after Normal and Pathological Labour.** (Les principaux facteurs de la sédimentation sanguine au cours de la grossesse et dans les suites de couches normales et pathologiques.)

By J. Badin and G. Conas. *Rev. Hémat.*, **2**, 296–304, 1947. 2 figs., 11 refs.

From the second or third month of pregnancy the erythrocyte sedimentation rate (E.S.R.) increases, reaching its maximum at term. The factors responsible for this acceleration are said to be: (1) a considerable increase in the amount of plasma relative to increase in the level of fibrinogen; (2) a qualitative change in fibrinogen; (3) a progressive increase in the "serum factor"; (4) a decrease in the number of erythrocytes. Normally, within 10 days of delivery the E.S.R. has returned to the level found between the fourth and sixth months of pregnancy. Infective complications—such as phlebitis or endometritis—cause great increase in the E.S.R., said to be due to increase in the serum factor, moderate increase in the plasma factor, and decrease in the number of erythrocytes. The authors reiterate the accepted teaching that such changes give an excellent indication of post-partum complications even before these are clinically evident. They point out that it is well known that the E.S.R. is accelerated after severe haemorrhage, but state that the determining factors are different, being, in order of importance, decrease in the number of corpuscles, increase in the plasma factor, and, of least importance, increase in the serum factor.

[This paper would seem to be one of the now numerous attempts to determine the bases of the erythrocyte sedimentation test, a praiseworthy aim, but one which, unfortunately, has led to continuous complication of what was originally a simple, but nevertheless valuable, test.] *A. Piney*

1439. **Behaviour of Single Fractions of Unsaturated Fatty Acids in the Blood Serum in Pregnancy.** (Sul comportamento delle singole frazioni degli acidi grassi insaturi nel siero della gravida.)

By G. Micale. *Riv. ital. Ginec.*, **30**, 36–48, 1947. 18 refs.

Applying the method of Allegra for determination of some fractions of unsaturated fatty acids the author has studied the behaviour of the oleic acid, linoleic acid, linolenic acid, and isolinolenic acid fractions in the blood serum of healthy pregnant women during the ninth month of pregnancy. As controls healthy non-pregnant women between 20 and 40 years of age were used. The blood samples were taken in the morning from fasting patients. The method is described in detail, and the results are tabulated. The values obtained revealed a constant increase in the fractions of unsaturated acids examined, more particularly in the oleic acid fraction.

Three possible hypotheses are considered. A foetal origin of the maternal unsaturated fatty acids is improbable. The increase in unsaturated acids cannot be due to an accumulation of the so-called vitamin F, since it involves not only those acids (linoleic and linolenic) to which a vitamin action has been assigned by Evans, but also the oleic acid. It is more probable that the increase is due to a deviation of the normal lipid metabolism. The author considers the possibility that the hyperlipaemia due to mobilization of the stored fats during pregnancy is preceded by a process of unsaturation of the fatty acids. *Rina Saunders*

1440. **Haemoconcentration in Obstetrics.** (La hemoconcentración en obstetricia.)

By L. T. Brousse and O. T. Rocchi. *Bol. Soc. chil. Obstet. Ginec.*, **12**, 302–310, Dec. 1947.

1441. **Haptoglobin in Obstetrics.** (Haptoglobin v porodnictive.)

By E. Dlhos. *Ceskoslov. Gynaek.*, **13**, 223–233, 1948. 11 refs.

1442. **Liver Function Tests in Pregnancy.** (Epreuves fonctionnelles et foie de grossesse.)

By D. Stucki. *Schweiz. med. Wschr.*, **78**, 487–491, May 22, 1948. 1 fig., 13 refs.

1443. **Tyrosine Tolerance Test in Pregnancy and the Puerperium.**

By E. W. Page. *Proc. Soc. exp. Biol., N.Y.*, **66**, 79–82, Oct. 1947. 2 figs., 7 refs.

Subjects employed for investigation of the tyrosine tolerance test included 8 women in normal pregnancy of 7 to 9 months' duration, 1 patient with eclampsia, and 1 with severe pre-eclampsia; 7 other women were studied from 1 to 36 hours after normal delivery. Ten control subjects of similar ages were selected. The fasting patient was given 4 g. of tyrosine in casein solution. Blood samples at two 45-minute intervals were examined by the method of Bernhart and Schneider (*Amer. J. med. Sci.* 1943, **205**, 636). In half the subjects of the normal non-pregnant and pregnant groups, urine samples were collected for 8 hours before and 8 hours after tyrosine administration. The samples were analysed for tyrosyl compounds (Medes, *Biochem J.*, 1932, **26**, 917). In this small series a

reduced tyrosine tolerance was found during pregnancy, but this condition was reversed after delivery. No changes in tolerance were noted in pre-eclampsia or eclampsia. It is thought that the observed shifts in tyrosine metabolism might invalidate the test as an indication of liver function in pregnancy and the puerperium.

Magnus Haines

1444. **Nucleolar Substance in the Anterior Lobe of the Human Pituitary Gland.**

By C. CAVALLERO. *Arch. Path.*, **44**, 639–645, Dec. 1947. 1 fig., 16 refs.

Large acidophil vesicles, possibly nucleoli, were found in the nuclei of chromophobe, eosinophil, and pregnancy cells, and in a few degranulated basophil cells of the anterior lobe of the pituitary body, most commonly in the marginal and posterior portions. The cells containing these vesicles varied in size from 10 to 35μ, with irregular nuclei most commonly of 15 to 22μ. The vesicles varied in size from 10 to 20μ; when they were small in relation to the nuclei containing them the chromatin of the latter was reticular, but when they were large the chromatin was condensed. The vesicles were not stained with specific stains for mucin, iron, fat, or lipids.

The vesicles were present in 34 per cent of 404 pituitary glands studied, and ranged in number from 1 to 5 per section; occasionally 5 to 10 and rarely 50 to 120 vesicles were found in a section. They are absent before puberty and most frequent between the ages of 20 and 40 years in both sexes. They were found in all patients during pregnancy and the puerperium, in female castrates, hypogonadic males, and in patients with gynaecomastia, adreno-genital syndrome, and Addison's disease. They were present in variable proportions of patients with a variety of diseases. Among non-endocrine diseases, the endonuclear vesicles are commonest in intracranial tumours, neoplasms, and leukaemia. It is suggested that the vesicles are giant nucleoli, concerned with a transfer of nuclear secretion to the cytoplasm. *G. Discombe*

1445. **Significance of Changes in the Anterior Lobe of the Pituitary in Pregnancy.** (Apropos du déterminisme et de la signification des modifications gravidiques de lobe antérieur de l'hypophyse.)

By L. DESCLIN. *Brux-méd.*, **28**, 1107–1112, May 30, 1948. 13 refs.

1446. **A Simplified Method for the Quantitative Determinations on Free Pregnanediol Excretion in Pregnancy.**

By M. E. DAVIS and N. W. FUGO. *Proc. Soc. exp. Biol. N.Y.*, **66**, 39–42, Oct. 1947. 1 fig., 5 refs.

Over 1,500 determinations of pregnanediol excretion have been carried out on a series of about 100 women attending the Chicago Lying-in Hospital. The method is an adaption of that described by Guterman (*J. clin. Endocrinol.*, 1945, **5**, 407), 100 ml. urine, 50 ml. toluene, 10 ml. concentrated hydrochloric acid, and a few glass beads being placed in a 500-ml. flat-bottomed Florence flask. The contents are boiled vigorously under a reflux condenser for 15 minutes on an electric hot-plate. After cooling under tap water to room temperature, the contents are transferred to a 500-ml. separating funnel, the urine-acid layer is drawn off and shaken twice with 10- to 15-ml. volumes of fresh toluene; the toluene emulsion layer in the separating funnel is then washed twice with 15-ml. portions of 0.1 N sodium hydroxide; this is followed by two washings with 15-ml. portions of distilled water. The washed toluene and toluene-water emulsion layers are transferred to a 125-ml. Erlenmeyer flask. A few glass beads are added with toluene rinsings to the funnel. The mixture is boiled on an electric hot-plate under a hood. When the toluene is boiling smoothly and after the emulsion layer has disappeared, 10 ml. of freshly prepared 2 per cent sodium hydroxide in absolute methanol is added slowly. Boiling is continued until a granular precipitate is obtained and the solution has turned yellow or greenish yellow. The toluene mixture is then filtered through medium porosity fritted glass filters under slight suction. The combined filtrates are evaporated on the hot-plate, an air stream being used to eliminate the last traces of toluene. To the residue is added 5 ml. of acetone. Solution is aided by gentle heat, and 20 ml. of 0.1 N sodium hydroxide is added slowly while the flask is still on the hot-plate. When the contents of the flask have boiled, the flask is placed in the refrigerator overnight. The resulting precipitate is collected by filtering through fritted glass and washed with the distilled-water rinsings. The precipitate is then washed with 10 ml. petroleum ether. The receiving flask is changed and the precipitate dissolved by passing 10 ml. of hot absolute ethanol through the funnel. Any reddish or yellowish discolouration of the precipitate necessitates re-precipitation by adding 40 ml. distilled water to the alcohol solution and heating to boiling. This step is repeated until the precipitate is white. The alcoholic filtrate is evaporated to dryness as above. To this 10 ml. sulphuric acid is added and the mixture allowed to stand for 1 hour. The fully coloured solution may require dilution before readings are made in the spectrophotometer. The authors demonstrate the accuracy of their method by gravimetric comparisons.

Magnus Haines

1447. **The Influence of Lowered Atmospheric Pressure on Pregnant Guinea-pigs.** (Vliv snížehého tlaku vzduchu na těhotna morcata.)

By J. MALEK. *Ceskoslov. Gynaek.*, **12**, 454–470, 1947. 2 figs., 11 refs.

Thirty-six pregnant and non-pregnant guinea-

pigs were exposed to low pressures corresponding to heights of 5,000 to 12,000 metres in a low-pressure chamber; 19 of them survived and gave birth to live animals, 11 of which were premature. Premature birth usually came on after 7 days. Six animals survived and had stillbirths. Five animals survived, each of which bore both live and dead litter. Six animals died, and it was found that the bigger the foetus the longer they survived a given pressure. Newborn animals were more resistant than both the foetus *in utero* and the pregnant adult animal. The author discusses the significance of his experiments for clinical medicine, with special reference to intrauterine asphyxia, the influence on pregnancy of sudden ascents to high altitudes, and the influence of climatic changes on pregnancy.

A. Rohan

1448. **A Multi-channel Strain-gage Tokodynamometer: An Instrument for Studying Patterns of Uterine Contractions in Pregnant Women.**

By S. R. M. REYNOLDS, O. O. HEARD, P. BRUNS, and L. M. HELLMAN. *Bull. Johns Hopk. Hosp.*, **82**, 446–469, Apr. 1948. 10 figs., 7 refs.

1449. **Some Local Factors in Placental Growth.** [In Russian.]

By E. N. PETROVA. *Akush. Ginek.*, No. 6, 23–26, 1947.

Beginning with a short account of an investigation into the biochemistry of "organizers" in amphibia, the author describes the results she obtained in a study of the metachromatic properties of human placental tissue. The results are based on the examination of 20 normal placentae (from 4 weeks to term) and of 3 abnormal placentae (2 cases of vesicular mole and 1 of chorionepithelioma). Metachromatic staining with toluidine blue of the stroma of the villi, just under the chorionic epithelium, is normally present in the first 3 months of pregnancy, and thereafter rapidly diminishes in extent, being absent at term. In hydatidiform degeneration and chorionepithelioma the amount of metachromatic tissue is significantly increased, and in chorionepithelioma the tissue is also present in the walls of the blood vessels supplying the growth.

Nicolas Tereshchenko

1450. **Possibility of Conception after the Bonney Amputation of the Cervix.** (Die konzeptionsmöglichkeit nach der flachen Portioamputation nach Bonney.)

By A. L. KROGER. *Zbl. Gynäk.*, **69**, 1110–1115, 1947. 6 refs.

1451. **The Friedman Test: A New Technique.** (Reação de Friedman por nova técnica.)

By N. DE CASTRO BARBOSA. *Rev. brasil. Med.*, **4**, 671–673, Sept. 1947.

Fifty ml. of fresh and filtered urine with 200 ml. of absolute ethyl alcohol is kept for at least half an hour at 37°C. The alcohol is then decanted and the sediment washed with approximately 5 volumes of sulphuric ether. The ether is decanted and the sediment is dissolved in 10 ml. of normal saline containing 1 to 2 drops of glacial acetic acid. After evaporation of the remaining ether, the solution is ready for injection into the auricular marginal vein of the female rabbit. By the original method 10 ml. of urine was injected; by this new method five times the quantity of hormone is introduced into the organism of the rabbit, producing an earlier follicular haemorrhage—within 24 hours instead of 48—even less in sensitive rabbits. In addition, by elimination of the fluid part of the urine, the risk of an immediate intoxication and death of the rabbit is avoided.

A. Lilker

1452. **Urine vs. Blood Serum in Friedman's Test for Pregnancy.**

By C. F. KENT. *J. Missouri med. Ass.*, **45**, 275, Apr. 1948.

1453. **Early Diagnosis of Pregnancy by "Prostigmin" Injection.** (La diagnosi precoce di gravidanza mediante iniezione di prostigmina.)

By M. FERRUZZI. *Ginecologia, Torino*, **14**, 105–120, Mar. 1948. 20 refs.

1454. **The Rapid Rat Test for Pregnancy. The Ovarian Hyperemia Response as a Routine Diagnostic Procedure.**

By G. M. RILEY, M. H. SMITH, and P. BROWN. *J. clin. Endocrinol.*, **8**, 233–243, Mar. 1948. 1 fig., 7 refs.

1455. **Pregnancy Test using the Male Toad.**

By C. GALLI MAININI. *J. clin. Endocrinol.*, **7**, 653–658, Sept. 1947. 4 refs.

A new biological test for pregnancy is described from Buenos Aires. On a basis of the relation described by Houssay and Gonzalez (*Rev. Soc. Argent. Biol.*, 1929, **5**, 77) between the pituitary of the male toad, *Bufo arenarum* Hensel, and its testis, the authors inject 10 ml. of first morning urine, untreated, into the lateral lymph sac of the toad. Urine (1 or 2 drops) is taken by pipette from the urinary bladder of the toad and examined microscopically. The appearance of spermatozoa 3 hours after the injection is evidence of a positive reaction. [Although only just under 100 cases have been investigated the thesis is well presented, Friedman (rabbit) tests having been carried out in parallel.] The authors made a large series of control injections of urine (male, female, and children's) and of a variety of hormones. Consistent results were obtained in 94 out of 99 urines. Inconsistent results are not analysed. The series is admittedly small and observations were made only in the summer months. [Provided there is no variation in relation to the season of the year and that the species of toad were available in other countries the diagnostic value of this toad test might become important.]

Magnus Haines

[See also Abstract 1456 for a description of the findings in a larger series.—EDITOR.]

1456. **The Galli Mainini Reaction.** (Consideraciones sobre la reacción de Galli Mainini.)

By R. M. PINTO and H. J. SUER BOERO. *Prensa méd. argent.*, **35**, 165–168, Jan. 23, 1948. 2 figs., 27 refs.

The results of the Galli Mainini test carried out 441 times on the urine of 255 patients are reported. The male toad, *Bufo arenarum* Hensel, was used. The animals weighed over 100 g. and several tests were carried out on the same toad at intervals of at least 4 days, as spermatozoa have been found in the urine in the cloaca up to 68 hours after the injection of the specimen, and even up to 7 or 8 days. The test is best performed on the morning urine, and the injection is made into the dorsal lymphatic sac in the midline, the needle being passed through the fibrous median raphe until the skin of the caudal region can be raised. The urine is withdrawn from the cloaca of the toad with a fine pipette, care being taken to avoid directing the pipette too deeply or too far anteriorly and thus obtaining intestinal contents.

In 158 cases of pregnancy it was found that if 2 test animals were used the percentage of positive reactions in the first 5 months was 100; if a single animal only was used the percentage was as low as 90 in the third month. The percentage of positive reactions reached its lowest between the sixth and seventh months, corresponding with the level of gonadotrophins in the blood. During labour the figure fell to 50 per cent, and almost to nil 48 hours after delivery. When 10 ml. of urine was used there were 11.55 per cent of negative reactions, but with 20 ml. only 3.15 per cent. In 16 cases the Galli Mainini and Friedman tests were carried out. In 3 both reactions were positive and in 4 both were negative. In 7 the Galli Mainini reaction was positive and the Friedman negative, and in 2 the Galli Mainini reaction was negative and the Friedman positive; in all of these cases the clinical findings supported the findings in the Galli Mainini test. After the expulsion of a hydatidiform mole, the Galli Mainini reaction becomes negative more quickly than do the Friedman and Aschheim-Zondek reactions. The minimum amount of chorionic gonadotrophin capable of giving a positive reaction, which is stated by other authors to vary between 10 and 30 international units, was found to be in the region of 10 to 14 units.

In 20 patients with gynaecological complaints and 45 with amenorrhoea of different kinds the test was always negative. No false positive reactions were observed. A dose of 20 ml. gave a more intense and sensitive reaction than did 10 ml., but was well tolerated only by animals injected for the first time. There was no mortality with doses of 10 ml. In pregnancy a positive reaction was obtained after only 5 days of amenorrhoea. The authors believe the Galli Mainini test to be one of the best of the biological tests for pregnancy because of its sensitivity, the simple technique and ease of interpretation, and because it renders early diagnosis possible.

Bryan Williams

1457. **The Galli Mainini Reaction in Diagnosis of Pregnancy.** (Diagnostico biológico del embarazo por la reacción de Galli Mainini.)

By S. FUENZALIDA, F. LILLO, and C. AGUILAR. *Bol. Soc. chil. Obstet. Ginec.*, **12**, 277–280, Nov. 1947. 5 refs.

1458. **Comparative Determinations of the Xenopus and Aschheim-Zondek Reactions.** (Xenopustest und Aschheim-Zondek'sche Reaktion.)

By E. EICHENBERGER. *Gynaecologia, Basel*, **125**, 337–347, June 1948. 3 figs., 22 refs.

1459. **Diagnosis of Pregnancy with the Common Frog** (*Rana esculeuta*). (Diagnostico del embarazo con la rana comun.)

By J. AZNAR-FERRERES. *Laboratorio, Granada*, **5**, 535–537, June 1948.

1460. **Colour Reaction of Pregnanediol and its Clinical Diagnostic Significance.**

By A. P. PREOBRAZHENSKY and G. V. ORDINETS. *Akush. Ginek.*, No. 6, 17–23, 1947.

After a brief review of the biochemistry of pregnanediol, the authors give a detailed account of the method of obtaining the colour reaction for pregnanediol. This reaction when positive is considered to afford fairly accurate confirmation of early pregnancy; as negative evidence this test is not so accurate as a negative Friedman or Aschheim–Zondek test. It is of value, however, in the prognosis of threatened abortion, and is a valuable and easy method of checking the effect of hormonal therapy in various menstrual abnormalities.

Nicolas Téreshchenko

1461. **Diagnosis of Sex in Utero by Hormonal Methods.** (Le diagnostic du sexe *in utero* à l'aide de méthodes hormonales.)

By I. BERTRAND and T. GAYET-HALLION. *Ann. Endocrinol., Paris*, **8**, 534–539, 1947. 28 refs.

1462. **Length of Human Gestation with Special Reference to Prematurity.**

By M. N. KARN. *Ann. Eugen., Camb.* **14**, 44–59, Oct. 1947. 4 figs., 25 refs.

From maternity hospital data the length of the human pregnancy (reckoned from the beginning of the last menstrual period) has been established as, on an average, 278 days, the standard deviation being 16.3 days; it has a wide range and includes about three times as many premature as post-mature births. The author assumes tentatively that the non-Gaussian distribution based on the raw data is composed of three curves, one for abnormal prematurity, one for natural full-term pregnancy (a normal curve) with mean 280 days and standard deviation 11.3 days, and one for abnormal post-maturity. A birth weight of under 5½ lb. (2.49

kg.), or 5¼ lb. (2.38 kg.) for females, together with a period of pregnancy of under 260 days, should be taken as an index of prematurity. The length of pregnancy is the same for successive pregnancies and for male and female babies. *H. Grüneberg*

1463. **Clinical Féatures and Treatment of Prolonged Pregnancy.** (Klinik und Therapie der übertragenen Schwangerschaft.)

By H. RUNGE. *Gerburtsh. u. Frauenheilk.*, **8**, 401–408, May 1948. 8 refs.

1464. **The Presumed Prolongation of Pregnancy.** (La supuesta prolongación del embarazo.)

By E. U. RODRIGUEZ. *Ginec. Obstet. Mexico*, **3**, 93–106, Mar.–Apr. 1948.

1465. **Roentgenologic Methods in Obstetrics.**

By M. SCHNEIDER. *Texas J. Med.*, **43**, 758–762, Apr. 1948. 8 figs., 7 refs.

1466. **Radiology as it Relates to Obstetrics.**

By R. D. MORETON and T. F. BUNKLEY. *Texas J. Med.*, **43**, 753–758, Apr. 1948. 5 figs., 14 refs.

1467. **Relation of Mothers' Diets to Status of their Infants at Birth and in Infancy.**

By L. W. SONTAG and J. WINES. *Amer. J. Obstet. Gynec.*, **54**, 994–1003, Dec. 1947. 1 fig., 12 refs.

The authors investigated the relation of mothers' diets to the status of their infants at birth and in infancy. McLester in 1943 stated that lack of protein in the mother's diet, unless extreme, will not affect the development of the foetus, the tissues of the mother being broken down to provide the necessary amino-acids. Yet in 1944 Burke, Harding, and Stuart concluded, from a study of 216 women and their children, that a significant relation was to be found between the protein content of the mother's diet during pregnancy and the length of her infant at birth. The authors' present study is based upon the observation of 205 mothers and their infants. These mothers, as a group, might be described as belonging to the upper middle class. Careful dietary records were obtained over considerable periods, and from these records quantitative analyses were made in terms of average intake of protein, calories, minerals, and the various vitamins. The mothers were divided into five groups, according to their daily intake of protein, the particular groupings being so devised as to correspond to those used by Burke *et al.* Anthropometric measurements, including crown–heel length, were made of all infants within 24 hours of their birth. As a result of these investigations the authors were unable to demonstrate unequivocally a relation between the mothers' diet and the length, weight, or ossification of their infants at birth or at 1 month, 6 months, and 12 months of age. They conclude that whilst maternal protein intake cannot be regarded as not having an effect upon the status of the infant at birth or during the first year, it must fall below the levels used in these groupings before such an effect is clearly demonstrable. Variations in technique may account to some extent for the considerable differences in results of their studies and those of Burke *et al.*

Falkland L. Cary

1468. **Nutrition in Pregnancy.**

By H. SIMONNET. *Canad. med. Ass. J.*, **58**, 556–561, June 1948. 8 refs.

1469. **Nutritional Requirements During Pregnancy and Lactation.**

By B. S. BURKE and H. C. STUART. *J. Amer. med. Ass.*, **137**, 119–128, May 8, 1948. 1 fig., Bibliography.

1470. **Proteins and Pregnancy.**

By J. H. HANNAN. *Med. Press*, **219**, 512–514, June 9, 1948. 6 refs.

1471. **Toxemia of Pregnancy.**

By S. T. GARBER and N. S. ASSALI. *J. Indiana med. Ass.*, **40**, 979–985, Oct. 1947. 1 fig., 13 refs.

The authors discuss the pathology and treatment of pre-eclampsia and eclampsia. The primary change is, they believe, vasoconstriction leading to ischaemia of the arteriolar and capillary wall with increased capillary permeability, oedema, and stasis, followed by damage to the endothelium and consequent thrombosis with or without haemorrhage, and finally, ischaemic necrosis in the area involved, the extent of the necrosis varying with the collateral circulation in the different organs. Intracranially, with the occurrence of increased pressure and vasospasm, there develop the classical signs of increased intracranial pressure—headache, vomiting, choked disk, convulsions, and coma. When a patient is seen for the first time late in pregnancy, observation of the eye grounds affords the best method of differentiating between hypertensive disease of long standing and pre-eclampsia. In the former the arterioles are constricted, tortuous, and of the silver-wire type, arterio-venous kinking is present, and the usual arterio-venous ratio of 2:3 is diminished to, for example, 1:2.

The following in outline is the therapy adopted: absolute rest in bed; forced fluids from 3,000 to 5,000 ml. daily; adequate protein intake; hypertonic glucose to promote absorption of oedema, secure diuresis, and supply glycogen to the liver; magnesium sulphate, intramuscularly to promote absorption of oedema, and by mouth to act as a saline cathartic. Magnesium sulphate is also given to decrease the irritability of the central nervous system. The authors do not employ sedatives, such as morphine, chloral, paraldehyde, barbiturates, to allay eclamptic convulsions because these only decrease the irritability of the nervous system and morphine inhibits the action of " veratrone "; the authors rely on veratrum viride " to reverse the vicious process initiated by vasoconstriction ".

Termination of pregnancy may be necessary to save the woman from permanent vascular damage, and it is thought that the risk of this depends less on the height of the blood pressure than on the duration of the hypertension. Termination is preferably delayed till 35 weeks and carried out from below by induction of premature labour. Caesarean section is performed when the cervix is not prepared for induction or when some other indication for it exists. The foetal mortality in the authors' series of 1,310 toxic cases was 9.8 per cent and in 40 cases of eclampsia 27.5 per cent. There were 4 maternal deaths (0.3 per cent). In 1 case death was due to sepsis, in 2 to haemorrhage, and in 1 to eclampsia. Severe toxic separation of the placenta occurred in 17 cases with 1 maternal death. For prophylaxis of pre-eclampsia the authors advocate good prenatal care and hygiene; excessive gain in weight must be avoided, and rest is essential. Adequate fluid intake is necessary and, to prevent oedema, sodium in the form of salt and soda must be restricted in the latter half of pregnancy. *F. J. Browne*

1472. **Clinical and Statistical Findings in 214 Cases of Toxaemia of Pregnancy.** (Rilievi clinico-statistici su 214 casi di tossiemia gravidica.)

By P. ALFIERI. *Ginecologia, Torino*, **13**, 367–390, Aug. 1947. 58 refs.

During the 10 years, 1934–43, there were 214 cases of toxaemia of pregnancy at the obstetrical and gynaecological clinic at Parma, representing 1.34 per cent of the pregnant women attending during this time. Of the total cases of toxaemia 55.6 per cent were seen in women aged 20 to 30, corresponding with the period of maximum fertility; primigravidae constituted 65.88 per cent of the patients. It was found that 35.5 per cent of the cases occurred in the spring and 26.5 per cent in the winter months — December, January, and February — while the lowest incidence was in autumn. In 54.2 per cent manifestations of toxaemia appeared for the first time in the last month of pregnancy, in 25.88 per cent in the eighth month. Albuminuria was present in every case. Hypertension, often reaching a high level, was found in the majority of cases.

During the second 5-year period, 29 per cent of patients were operated upon, compared with 32.14 per cent in the first 5-year period. Operative procedures, which were carried out with as little trauma as possible, included the use of Krause's bougies, extraction with forceps, or internal version. In the first 5-year period 5 mothers died, and necropsy revealed a degenerative lesion of the kidneys. In the second 5-year period only 1 patient died—of cerebral haemorrhage. Maternal mortality was 5.9 per cent in the first 5-year period and 3 per cent in the second; foetal mortality was 28.57 and 26.15 per cent in the two periods respectively. The author claims that the improvement in the second 5-year period may be attributable to a method of treatment in which glucose, insulin, and folliculin were employed. Eclampsia was treated by the method of Stroganoff in the first 5-year period, while in the second "pernocton" and sodium dehydrocholate were used. The author believes that treatment with hormones, especially folliculin, is of value, and suggests that toxaemia may be a result of hormonal imbalance in the mother, caused by the secretions of the chorionic tissue.

[The diagnosis of toxaemia in this series of cases appears to have been made solely on the occurrence of albuminuria. It seems that blood pressure was not recorded until albuminuria had appeared. This makes the results hardly comparable with those from Britain, where, on the whole, the importance of a rise in blood pressure as an early sign of toxaemia is appreciated. The statistical evidence in this article does not appear to be adequate to prove that the newer methods of treatment employed were effective.] *Josephine Barnes*

1473. **Aetiology of Toxaemia of Pregnancy.** (Graviditetstoxemiens etiologi.)

By A. EDLEN, B. KNUTSSON, and K. PALMSTIERNA. *Nord. Med.*, **36**, 2281–2285, Nov. 14, 1947. 7 refs.

At the County Hospital in Sundsvaal, Sweden, during the period July 10, 1947, to Aug. 20, 1947, the blood groups of 129 mothers admitted to the obstetrical unit were determined. Many of the babies and their fathers were examined in the same way. Of 31 mothers, the fathers of whose infants belonged to blood group O, only one showed any sign of toxaemia of pregnancy. In 59 cases in which the father and mother belonged to the same blood group and in 7 cases in which the mother belonged to group AB there was also no toxaemia. In 11 cases of toxaemia, the blood groups of father and mother were different, the father's group being A, B, or AB, and the mother's group O, A, or B. In some of these cases the infant and its mother belonged to the same group.

It is thought probable that toxaemia of pregnancy depends on two factors, the hypertrophy of hypophysis and thyroid normally associated with pregnancy and an extraneous factor depending on the blood group to which the father belongs. If he belongs to group O or the mother to group AB, or if both belong to the same blood group, the pregnancy is regarded as homologo-specific. All other pregnancies are considered hetero-specific, and it is in these that toxaemias of pregnancy develop, notably when the mothers are primiparae. On the assumption that toxaemia of pregnancy is an allergic reaction depending on the character of the father's blood, desensitization of the mother with intracutaneous injections of the father's blood is recommended early in pregnancy when the latter has been found to be hetero-specific. Such desensitization must be started before injury to the

vascular system has become serious. A report on the results of these prophylactic measures is promised in the near future. *Claude Lillingston*

1474. **Serologic Observations in the Toxemias of Pregnancy.**

By R. T. La Vake. *Minnesota Med.*, **31**, 372–375, Apr. 1948.

1475. **Clinical Investigations and Considerations on the Influence of the War Years on Pregnancy. II. Influence on Toxaemias of Pregnancy: Albuminuria.** (Indagini cliniche e considerazioni circa l'influenza del periodo bellico sullo stato puerperale. II. Influenza sulle tossicosi gravidiche: Albuminuria.)

By S. Canna. *Ginecologia, Torino*, **13**, 430–442, Sept. 1947. 4 figs., 47 refs.

A comparative clinical and statistical survey has been made of the incidence of albuminuria, toxic neuritis, and icterus gravis in pregnancy during the periods of peace and war between 1933 and 1945 in Novara. Albuminuria was the more frequent form of toxaemia, while toxic neuritis and icterus made up a very small percentage. The curves of frequency of all these toxic manifestations were similar and for this reason the author has considered them as a whole. The relations between toxaemias and primiparity or multiparity, living conditions, and occupation during pregnancy have been investigated.

A maximum of 8.3 per cent of toxic manifestations was found in 1934 among 635 deliveries and a minimum of 1.3 per cent in 1945 among 577 deliveries. In the period between 1933 and 1939 the average was 6.5 per cent (4,523 deliveries) and in the period between 1940 and 1945, 2 per cent (4,113 deliveries). An average of 8.7 per cent was found in peacetime among primigravidae (1,958 deliveries) and 2.8 per cent in wartime (1,830 deliveries); the figures for multigravidae were 5 per cent (2,555 deliveries) and 1.4 per cent (2,283 deliveries) respectively. Women living in the country had better food than those living in towns. For urban patients the average incidence was 5.8 per cent in peacetime (2,305 deliveries) and 2.3 per cent in wartime (2,214 deliveries); for those from the country the figures were 7.4 per cent (2,218 deliveries) and 1.8 per cent (1,949 deliveries). Toxic manifestations were found in 7 per cent of women who did only housework during pregnancy in peacetime (1,949 deliveries) and in 2.8 per cent in wartime (2,116 deliveries); in 5.5 per cent of factory workers in the first period (1,665 deliveries); and in 1.4 per cent during the second (1,327 deliveries); in 9.5 per cent of landworkers in the first period (908 deliveries), and in 0.9 per cent in the second (660 deliveries). Since fewer land workers attended the Obstetric Clinic of Novara during the war these percentages cannot be regarded as conclusive.

From this investigation it appears that there was a decrease in toxic manifestations during the war. The percentage was slightly lower for multiparae than for primiparae. The decrease was more noticeable among women living in the country and among land workers. The factors which may have caused these phenomena are discussed. It is the author's opinion that the nutritional factor is important in this decline in incidence of toxaemia. Carbohydrates, vegetables, and fruit figured prominently in the diet of pregnant women in the province of Novara, while animal protein and lipids were less than in peacetime.

Rina Saunders

1476. **A Case of Toxic Pyelonephritis of Pregnancy Cured by Infiltration of the Renal Pedicles and Medical Treatment.** (Sur un cas de pyélonéphrite gravidotoxique guérie par infiltration des pédicules rénaux et traitement médical.)

By R. Mahon and —. Chastrusse. *Rev. franç. Gynéc.*, **42**, 324–333, Nov. 1947. 1 fig., 15 refs.

The authors describe a case of toxic pyelitis of pregnancy in a primigravida, due to *Bacterium coli*, which persisted after delivery and was still present in a second pregnancy. The patient's general condition was poor; there was much wasting, necessitating the administration of glucose and insulin. At the onset of her illness there was oliguria with azotaemia, severe anaemia, and jaundice. The first pregnancy terminated in spontaneous delivery of a living child at the eighth month. At the height of the oliguria, and after intravenous procaine had proved ineffective, the renal pedicles were infiltrated with 20 ml. of 1 per cent procaine on both sides. This resulted in satisfactory diuresis. [This patient also received a large dose of penicillin, 800,000 units in all. This appears to have been given without a penicillin-sensitivity test on the organism, and there is no record of any trial of sulphonamides, which are usually more effective in cases of this kind.] *Josephine Barnes*

1477. **Renal Manifestations of Toxaemia of Pregnancy.** (Las manifestaciones renales de la gestosis.)

By V. Marino Donato. *Sem. méd.*, **55**, 879–884, May 27, 1948.

1478. **The Influence of Toxaemias of Late Pregnancy on the Fate of the Foetus.** (Der Einfluss der Spätschwangerschaftstoxikose auf das kindliche Schicksal.)

By V. Dubrauszky and E. Ott. *Geburtsh. u. Frauenheilk.*, **8**, 376–384, Apr. 1948.

1479. **Elevated Blood Pressure in Pregnancy. A Report of 1,800 Cases.**

By W. F. Dillon and H. E. Schmitz. *Amer. J. Obstet. Gynec.*, **54**, 948–957, Dec. 1947. 1 fig., 1 ref.

The authors take 140/90 mm. Hg as the standard of normal blood pressure. From 1931 to 1945 inclusive 28,263 women were delivered at the Lewis Maternity Hospital, Chicago. Of these, 1,800, or

6.36 per cent, had a blood pressure of or over the above standard during all or a part of their pregnancy. Pre-eclampsia was present in 5.14 per cent, eclampsia in 0.18 per cent, nephritis in 0.04 per cent, and hypertension in 1.0 per cent; 3.4 per cent of the pre-eclamptic patients progressed into eclampsia. In the pre-eclamptic group the percentage of primiparae was 52 and of multiparae 48; in the eclamptic group the percentages were primiparae 80 and multiparae 20. The nephritic group contained 50 per cent of each; and of the hypertensive patients 25 per cent were primiparae and 75 per cent multiparae. In 90 per cent of each group the rise in pressure was first demonstrated after 30 weeks. Of the eclamptic group there was headache in 70 per cent, epigastric pain in 32 per cent, visual disturbance in 46 per cent, and albuminuria in 98 per cent. The convulsions were antepartum in 35 per cent, intrapartum in 33 per cent, and postpartum in 31 per cent. Among the 51 eclamptics there were 4 maternal deaths and 25.3 per cent of the babies were stillborn or died in the neonatal period.

Treatment is discussed in some detail. All normal patients are given an 1,800-calorie diet made up of 85 g. protein, 75 g. fat, and 200 g. carbohydrate. A salt-free diet containing 85 g. protein is instituted with sedatives and enteric-coated tablets of ammonium choride, 1½ to 6 g. daily, if the pressure begins to rise and the weight to increase suddenly. Absolute rest in bed in hospital is indicated if the blood pressure remains over 140/90. Hypertonic glucose in water, sedatives, and parenteral magnesium sulphate are used in amounts commensurate with the severity of the toxaemia. For the eclamptics medical measures are employed. If the pregnancy must be terminated because of failure to respond to medical treatment and the cervix is in a state which contra-indicates delivery from below, Caesarean section is carried out under local analgesia.

Dieckmann, in discussing this paper, said that in his clinic the incidence of toxaemia had not decreased in the last 10 years. Eclampsia, however, had almost disappeared and at most there was only 1 case a year. "As the doctors in the clinic become more experienced watching for excessive weight gain, for increases in systolic blood pressure, our results in the treatment of these toxaemic patients improve. The patients are put under dietary control and bed rest at an earlier date."

F. J. Browne

1480. **The Significance of Hypertension in Pregnancy.**

By L. F. RITMILLER, I. L. MESSMORE, and R. E. NICODEMUS. *Pennsylvania med. J.*, **51**, 771–775, Apr. 1948. 6 refs.

1481. **Diminished Incidence of Eclampsia during the War and Post-War Increase.** (Verminderling van eclampsie tijdens de oorlog en toeneming daarvan na de oorlog.)

By W. VAN ESSEN. *Ned. Tijdschr. Geneesk.*, **91**, 3629–3633, Dec. 13, 1947. 1 ref.

In Deventer (Holland) among 3,174 confinements during the war years 1942–4 not a single case of eclampsia occurred; in 1946, out of 1,339 confinements, there were 6 cases and 2 of the mothers and 5 of the infants died. The average daily intake of protein during the war years was 100 to 120 g., a restricted amount but still within the normal limits. On the other hand, there was a scarcity of salt, the consumption of which, particularly among the rural population, was very low. The absence of eclampsia is attributed by the author to the low salt intake, and he advises a low-salt diet as the main precaution where this condition is feared. *A. Lilker*

1482. **New Electrocardiographic Observations in Eclampsia and Pre-eclampsia.** (Neue elektrokardiographische Untersuchungen bei der Eklampsie und ihren Vorstadien.)

By G. MESTWERDT. *Zbl. Gynäk.*, **69**, 759–765, 1947. 4 figs., 31 refs.

In eclampsia and pre-eclampsia changes in the capillaries are constantly found. The electrocardiographic observations carried out by the author revealed functional disorders of the cardiac muscle, probably due to functional disorders of the cardiac capillaries. He advocates periodic electrocardiographic control during pregnancy in the early diagnosis of pre-eclampsia and eclampsia.

Kate Winkler

1483. **The Treatment of Eclampsia and Pre-eclampsia with Veratrum Viride and Magnesium Sulfate.**

By F. C. IRVING. *Amer. J. Obstet. Gynec.*, **54**, 731–737, Nov. 1947. 1 fig., 22 refs.

Bryant in 1935 (*Amer. J. Obstet. Gynec.*, **30**, 46) reintroduced veratrum viride into the therapeutics of obstetrics. He reported its use in a series of 121 cases of eclampsia with a mortality of 9.9 per cent. In view of Bryan's paper the author decided to use his technique at the Boston Lying-in-Hospital. The pharmacology of the drug is discussed, and a historical review of its use is followed by a description of the technique of administration. Patients on admission are given either morphine gr. ¼ (16 mg.), pethidine 100 mg. or paraldehyde 3 drachms (10.5 ml.) as a sedative, and 5 minims (0.3 ml.) of "veratrone"; 10 to 20 ml. of 50 per cent magnesium sulphate is administered intramuscularly every 4 to 6 hours and 250 ml. of 25 per cent glucose intravenously every 4 to 6 hours. The veratrone in 5-minim doses is repeated every 25 minutes to keep the systolic blood pressure below 150 mm. Hg. From 1940 to 1946, 32 patients with eclampsia were treated in this way. There were 2 maternal deaths (6.3 per cent). Half the total number of patients treated were admitted as emergencies; 18 of the 33 infants born were discharged alive (54.5 per cent).

A graph demonstrates the maternal mortality from eclampsia for the preceding 70 years (the average percentage death rate per year being 28.3). A table also shows different authors' results with magnesium sulphate treatment, with or without veratrone. Results obtained with veratrone appear to be better than those obtained with magnesium sulphate alone. *Braithwaite Rickford*

1484. **Fatal Eclampsia. A Clinical and Anatomic Correlative Study.**

By G. T. C. WAY. *Amer. J. Obstet. Gynec.*, **54**, 928–947, Dec. 1947. 9 figs., 59 refs.

This paper summarizes the postmortem findings in 33 cases of eclampsia. In 8 of the cases there were no convulsions; 32 of the patients had hypertension, blood pressure varying from 140 mm. systolic to over 200. One patient was in shock on admission and the blood pressure was 80/40 mm. Hg. Generalized oedema was present in 78 per cent of the patients on admission, and 69 per cent were in coma. The author is not impressed by the tubular changes in the kidney. The glomerular changes he describes in 3 stages: (1) Non-vascular glomeruli, increase in glomerular nuclei, moderate thickening of basement membrane, no visible changes in arterioles. (2) Non-vascular glomeruli, increase in glomerular nuclei, arteriolar thickening, marked thickening of basement membrane, fibrinoid changes in glomeruli and arterioles. (3) Scattered obliterated hyalinized glomeruli, fibrosis beneath Bowman's capsule, generalized arteriolosclerosis, kidney of arteriolo-nephrosclerosis. Six of the cases were in stage 3. An analysis of the cases in each stage showed that the proportion of primiparous patients fell from 82 per cent in stage 1 to 50 per cent in stage 2, and to 0 in stage 3. Also, with one exception, the findings in multiparae with a history of preceding toxaemia were confined to stages 2 and 3. The average age for each group rose from 19.3 years to 30.8 in the progressive stages of renal injury. The average duration of symptoms in all stages was practically the same—26.6, 25.3, and 28.4 days.

In the adrenals the chief findings were necrosis and haemorrhage. These lesions were present in 11 patients; in 5 they were so severe that practically no functional adrenal cortical tissue remained. It is emphasized that normal blood pressure in toxaemic patients does not preclude the presence of shock, and that after marked hypertension a reduction to normal levels may be coincident with the existence of the shock syndrome. It is suggested that adrenal insufficiency may be a contributing factor to a fatal termination in certain patients. Pneumonia was present in 16 cases and bilateral hydrothorax in 1 case. There were haemorrhages in the heart in 12 patients and in 4 of these there was focal necrosis of the myocardium. Myocarditis was seen in 2 cases and focal acute endocarditis in one. Focal necrosis of the brain was present in 1 case and cerebral haemorrhage in 3 cases, in 2 of which it was massive; in these 2 cases there was cerebral arteritis and arteriolitis with necrosis of the vessel walls. Acute purulent mastitis was found in 1 case, and this had been followed by eclampsia and death in 36 hours after the first symptom.

The author considers that the underlying cause of all these lesions is the vasoconstriction. This he attributes tentatively to the euglobulin toxic factor found in menstrual flow by Smith and Smith, and which can also be produced in any area where there is tissue destruction, such as might arise in a focus of infection or in a senile placenta. The lethal action of the toxin may be assisted by the increased sensitivity of the vascular system which has been shown to be present in pre-eclampsia toxaemia and to be acquired at some time after the seventeenth week of pregnancy. The increased incidence of eclampsia in patients with pre-existing chronic hypertension might be due to the fact that uterine vascular changes bring about a relatively inadequate uterine blood supply and in turn premature senile changes in the placenta.

[The abstracter ventures to suggest that the hypertension with resultant vascular spasm in the spiral arterioles of the decidua may produce haemorrhages and tissue destruction. From such destroyed areas, either in the decidua or in the placenta, the lethal substance (necrosin?) may arise. This hypothesis brings us very near to Young's views on the aetiology of eclampsia (*vide Proc. R. Soc. Med.*, 1914, **7**, Sect. Obstet. Gynaec., 307). The difficulty in all existing theories is to explain why eclampsia occasionally occurs 3 or 4 days after the placenta is delivered.]

F. J. Browne

1485. **Employment of Aqueous Solution of Adrenal Cortex Hormone in a Case of Eclampsia.** (Použití vodného roztoku hormonu kory nadledvinkové u pripadu eklampsie.)

By M. VOJTA. *Ceskoslov. Gynaek.*, **13**, 233–240, 1948.

1486. **Postpartum Eclampsia.** (A propos de l'éclampsie du post-partum.)

By E. HOUEL and H. ÉZES. *Gynéc. et Obstét.*, **47**, 330–334, 1948.

1487. **Treatment of Vomiting of Pregnancy with Amino-acids.** (Essai thérapeutique des vomissements gravidiques par les acides amines.)

By H. FOBE. *Therap. Umsch.*, **5**, 33–37, June 1948. 23 refs.

1488. **Placenta Previa.**

By A. L. DIPPEL. *Amer. Practit. Phila.*, **2**, 597–602, May 1948. 4 figs., 4 refs.

1489. **Treatment of Placenta Praevia.** (Consideraciones sobre tratamiento de la placenta previa.)

By J. R. GONZALEZ. *Bol. Soc. chil. Obstet. Ginec.*, **12**, 310–326, Dec. 1947.

1490. **The Pathological Physiology of Acute Loss of Blood in Pregnant and Non-pregnant Women.** (Zur Pathophysiologie des akuten Blutverlustes bei Frauen mit und ohne Schwangerschaft.)

By H. SCHWALM. *Arch. Gynäk.*, **176**, 70–99, 1948. 8 figs., 48 refs.

1491. **A Premature Survival Index and the Conduct of Premature Labor.**

By A. L. DIPPEL, H. W. JOHNSON, and J. L. CORNELISON. *Amer. J. Obstet. Gynec.*, **54**, 1004–1012, Dec. 1947. 9 refs.

The authors survey the definition of the premature infant, offer a " premature survival index ", and suggest certain rules for the conduct of premature labour. There is no unanimity of opinion on what constitutes a premature infant, and no standard is universally accepted. Many factors are involved in the assessment of the term. One of the authors (Johnson) suggests that a combination of a large number of the factors concerned in the term "prematurity " should give rise to less inaccuracy than has so far resulted from the use of one factor alone. The suggested index is based upon five points: gestational period; weight of the newborn child in ounces; total or crown–heel length of the infant; occipito-frontal circumference of the head, recorded in inches; and the circumference of the chest at the level of the xiphisternal joint, also recorded in inches. The recorded figures for each of these measurements or factors, divided by five, give the index figure. The authors have applied their standard to 23 premature infants, and, while pointing out that the number of cases is too small to permit of permanent conclusions being drawn, suggest that certain useful information is already forthcoming from the method. Their suggestions for the reduction of the mortality rate in premature infants include the avoidance of analgesia after the onset of true labour; the use of local or regional analgesia for delivery; preservation of the membranes throughout the second stage of labour; the maintenance of the maternal–foetal circulation for as long a period as possible; and the prophylactic use of chemotherapy in the premature child irrespective of any antenatal or intrapartum infection. *Frankland L. Cary*

1492. **Influence of Endogenous Factors (Ovarian Insufficiency) and Exogenous Factors (Profession) on the Origin of Premature Labour.** (Der Einfluss endogener Faktoren (Ovarialinsuffizienz) und exogener Faktoren (Berufsarbeit) auf die Entstehung von Frühgeburten.)

By H. KIRCHHOFF. *Geburtsh. u. Frauenheilk.*, **7**, 78–86, Nov. 1947.

Although since 1901 mortality during the first year of life has fallen considerably, mortality at birth and in the following 10 days has not decreased proportionately. In 14,564 pregnancies in Leipzig there was a primary infant mortality of 5.4 per cent (antepartum, intrapartum, and postpartum); 25.5 per cent of deaths were associated with prematurity; 33 per cent took place during labour and 41.5 per cent within the first 10 days of life. Birth trauma accounted for 30 per cent of all the deaths and placental abnormalities and lesions of the cord for 23 per cent. The author found that about 50 per cent of all deaths were associated with a birth weight of 2.5 kg. or under, and 60 per cent with a weight below 2.8 kg. Although some of these deaths may be explained by developmental abnormalities, the majority are due to unknown factors. It was previously noted in Leipzig (1933–37) that 52 per cent of mothers who gave birth to premature infants had symptoms of genital hypoplasia or ovarian insufficiency, and these are considered important endogenous factors in premature birth and associated foetal mortality. A further influence may be the social status of the mother and whether or not she works during the pregnancy. Some 13,000 cases were examined from this point of view; 40 to 50 per cent of pregnant women were found to be at work in different years of the analysis. In those who worked the percentage of premature births was 15.2, in those who did not work 10.5; detailed analysis showed varying percentages according to the type of work done (for example, 17.2 per cent in industrial factory workers, and 11.8 per cent in those working in hotels). In the working group the membranes ruptured prematurely in 41 per cent of all births compared with 30 per cent in the other group. Premature labour was less common if there was a period of rest at the end of the pregnancy; in those who did not rest the percentage of premature births was 26 to 36, compared with 6.5 to 10 per cent in patients who did not " work " for 70 to 90 days before delivery. It appeared that birth weights were higher in the " resting " group and that pregnancy was prolonged slightly in the industrial worker. *Kenneth Bowes*

1493. **Causal Connexion Between Repeated Abortion and Premature Labour and Pathological Spermatozoa.** (Uber die Frage eines ursächlichen Zusammenhanges zwischen wiederholten Fehl- und Fruhgeburten und krankhaftem Sperma.)

By P. ROTTGER. *Zbl. Gynäk.*, **69**, 1133–1139, 1947.

1494. **Preservation of the Threatened Pregnancy with Particular Reference to the Use of Diethylstilbestrol.**

By G. ROSENBLUM and E. MELINKOFF. *West. J. Surg. Obstet. Gynec.*, **55**, 597–603, Nov. 1947. Bibliography.

There is little doubt that abortion is heralded by a drop in the level of pregnandiol excretion in the urine, which is presumed to indicate a reduced progesterone content in the blood, but there is some evidence that an attempt to remedy this by the

administration of progesterone further reduces the output of pregnandiol. This effect can be avoided if oestrogens are given at the same time. Oestrogen therapy alone might be expected to be equally effective, since it prevents regression of the corpus luteum when injected into rabbits and causes enlargement of both follicles and corpora lutea in hypophysectomized rats. Administration of oestrogens to pregnant women increases the output of progesterone. Abnormal metabolism of the sex steroids begins during the second trimester, so that endocrine treatment must be started by the sixteenth week.

Diethylstilboestrol was given in 96 cases of threatened abortion, habitual abortion, and threatened premature labour. At the onset of symptoms of abortion the patient was sent to bed and given 5 to 25 mg. diethylstilboestrol orally, 25 mg. every hour until symptoms subsided, and thereafter 5 mg. three times daily until at least the twentieth week. In threatened premature labour 25 mg. was given hourly until contractions ceased, then 5 mg. three times daily until the thirty-sixth week. In habitual abortion 5 mg. was given three times daily until the twentieth week, when the dose was increased by 5 mg. weekly until the thirty-sixth week and then discontinued. In addition, all received the usual vitamin and mineral supplements and " rather frequent . . . small doses of thyroid ". No important toxic effects were noted; some mothers and babies showed transitory pigmentation of the areola and linea nigra. Two mothers had toxaemia. All the babies survived except 1 with multiple deformities. The results of the investigation are shown in the following table:

Condition	Stilboestrol			Progestogens		
	No.	Carried	Aborted	No.	Carried	Aborted
Threatened abortion	82	71 (86.6%)	11 (13.4%)	86	56 (65.1%)	30 (34.9%)
Habitual abortion	10	5 (50%)	5 (50%)	7	2 (28.6%)	5 (71.4%)
Threatened premature labour	4	3 (75%)	1 (25%)	1	0	1 (100%)

The author states that these results are better than any he has been able to achieve with other methods. There are several questions relating to the use of the oestrogens which require further investigation—for example, the possibility of producing permanent glandular disturbance in mother or child and the carcinogenic effect of such large doses. [A comprehensive bibliography of the literature relating to the endocrine aspects of abortion is appended.] *Margaret Puxton*

1495. **Interruption of Pregnancy.** (Nogle Bemærkninger om Svangerskabsafbrydelse.)

By J. FABRICIUS-MOLLER. *Ugeskr. Læg.*, **110**, 721–724, June 17, 1948.

1496. **The Blood Phosphatase During Abortion.** (Etude de la phosphatasémie au cours des avortements.)

By R. BURTHIAULT, R. BERGER, and J. GONNET. *Gynéc. et Obstét.*, **47**, 347–348, 1948.

1497. **Therapeutic Abortion from the Point of View of the Internist.**

By H. M. KORNS. *J. Amer. med. Ass.*, **137**, 333–336, May 22, 1948. 2 refs.

1498. **Indications for Therapeutic Abortion from the Point of View of the Surgeon.**

By S. C. HARVEY. *J. Amer. med. Ass.*, **137**, 331–332, May 22, 1948. 6 refs.

1499. **Therapeutic Abortion by Means of Soft-Soap Pastes.**

By H. H. F. BARNS. *Lancet*, **2**, 825–827, Dec. 6, 1947. 3 figs., 4 refs.

To induce therapeutic abortion the author has used a soft-soap paste containing stearic acid 10 per cent, arachis oil 20 per cent, alkaline solution (potassium hydroxide 9.5 parts, sodium hydroxide 3.75 parts; and water to 100 parts) 20 per cent, " lanette wax " 1.5 per cent, chlorocresol 0.05 per cent, and water to 100 per cent; the paste is sterilized in the autoclave. No anaesthetic is required for its injection, which is made between the membranes and the wall of the uterus with a 20-ml. syringe and a Forsdike intrauterine tube. One ml. is used for each week of pregnancy plus 5 ml. to allow for the quantity in the tube itself. Because success is uncertain, the paste should not be employed if the pregnancy has lasted more than 16 weeks; neither should it be used before 10 weeks, as the ovum has not obliterated the cavity of the uterus. The method was successful in 80 per cent of a total of 71 cases. There were no fatalities and no accidents such as have been described in the literature—haemolysis, perforation of the uterus, septic infection, and haemorrhage. Abortion usually took place within 24 to 48 hours and in most cases was complete, but in a few it was incomplete, and ecbolics were required to complete it. In 1 patient who was 16 weeks pregnant the paste was mixed with a radio-opaque substance " neohydriol ". X-ray examination showed some of the paste in the Fallopian tube and, 4 days after the abortion, in the pelvic portion of the peritoneal cavity. It is concluded that the method, in suitable cases, compares favourably with other methods of terminating early pregnancy. It has the great advantages that no general anaesthetic is required, the procedure only takes a few minutes, and there is a minimum of manipulation with little or no loss of blood. *F. J. Browne*

1500. **Cerebral Accidents during Abortion Provoked by Intrauterine Injection.** (Accidents cérébraux au cour d'un avortement provoqué par injection intra-utérine.)

By R. ROUCHY. *C. R. Soc. franç Gynéc.*, **18**, 78–80, Mar. 1948.

1501. **Uterine Necrosis Due to Intrauterine Injections of Soap-suds.** (A propos de six cas d'infarctus utéro-annexiel ou nécrose alcaline de l'utérus par injection intra-utérine d'eau de savon.)

By A. TURRETTINI. *Praxis*, **37**, 343–349, May 13, 1948. 7 refs.

1502. **Ligation of the Inferior Vena Cava and Ovarian Veins for Infected Abortion.**

By H. F. NEWMAN. *Amer. J. Surg.*, **75**, 746–748, May 1948. 4 refs.

1503. **Cervical Fibroids and Pregnancy.** (Cervikální myomy a těhotenství.)

By A. KOTASEK. *Ceskoslov. Gynaek.*, **13**, 191–197, 1948. 2 figs., 10 refs.

1504. **Pregnancy and Ovarian Cyst.** (Gravidez e cisto do ovario.)

By P. OSORIO. *Hospital, Rio de J.*, **33**, 621–631, Apr. 1948. 4 figs., 9 refs.

1505. **Acute and Chronic Intoxications in Pregnancy.** (Intoxicaciones agudas y crónicas en relación con la gestante.)

By L. A. BUENAPOSADA. *Clin. y Lab.*, **45**, 438–443, June 1948. 10 refs.

1506. **Phaeochromocytoma in Pregnancy.** (Een phaeochromocytoom in de zwangerschap.)

By A. J. A. HOOGEVEEN. *Ned. Tijdschr. Geneesk.*, **92**, 1681–1690, June 5, 1948. 10 refs.

1507. **Peptic Ulcer and Pregnancy. Four Cases and a Review of the Literature.**

By S. P. BRALOW, S. SCHEINBERG, and H. NECHELES. *Amer. J. digest. Dis.*, **15**, 137–141, May 1948. Bibliography.

1508. **Intestinal Obstruction Complicating Pregnancy.**

By S. A. SIEGEL and N. PLESHETTE, *N.Y. St. J. Med.*, **48**, 1264–1267, June 1, 1948. 13 refs.

1509. **Appendicitis in Pregnancy (Considerations on the Cases at the Obstetric Clinic, Pavia, from 1935–1946).** (L'appendicite in gravidanza. Considerazioni sulla casistica del decennio 1935–46 nella Clinica Ostetrica di Pavia.)

By G. PICINELLI. *Monit. ostet.-ginec.*, **18**, 97–124, Jan.–June 1947. 34 refs.

The author presents a clinical and statisical survey of the cases of appendicitis seen at the Obstetric Clinic of Pavia in the last 10 years. Among 9,664 pregnant women admitted, appendicitis was encountered 24 times—23 of the patients had chronic and subacute forms and 1 had acute appendicitis. The low incidence of acute appendicitis is related to the routine performance of appendicectomy early in pregnancy in mild cases, so as to avoid complications later on. Appendicitis was encountered four times in the second month of pregnancy, six times in the third month, seven times in the fourth, twice in the fifth, twice in the seventh, and three times during labour.

Appendicectomy was performed during pregnancy twenty-one times. Administration of morphine and abdominal application of an ice-bag was the routine after each operation. In 16 patients pregnancy continued without any disturbance. Of the other 5, 1 who was pregnant at the seventh month had a premature delivery with a living infant 7 days after the operation, Porro's operation was performed during labour in 3 cases (living infants), and 1 woman aborted 36 days after operation. Appendicectomy was performed in the other 3 cases a few days after the women had aborted. Two of these were admitted with threatened abortion and 1 with missed abortion. The postoperative period was uneventful in all cases.

In a discussion all the speakers agreed that acute appendicitis during pregnancy always has a bad prognosis, and that the foetal and maternal risk is high, especially in the late months of pregnancy, and above all during labour. The author urges that appendicitis during pregnancy requires operation as soon as possible. The early adoption of Porro's Caesarean section is suggested for the treatment of acute appendicitis during labour.

Rina Saunders

1510. **Pregnancy Complicated by Transmesenteric Hernia.**

By J. M. MILLER. *Amer. J. Surg.*, **75**, 739–742, May 1948. 7 refs.

1511. **Observations on the Occurrence of Anemia in Pregnancy.**

By W. KOCH, D. KAPLAN, and A. SADOVSKY. *Med. Rec., N.Y.*, **161**, 223–225, Apr. 1948. 2 figs., 3 refs.

1512. **A Case of Sickle Cell Anemia Complicating Pregnancy.**

By W. J. FETTER. *Bull. Sch. Med. Maryland*, **32**, 210–214, Apr. 1948. 1 fig., 14 refs.

1513. **The Rh Factor in Clinical Obstetrics and Gynecology.**

By J. W. DAVENPORT. *New Orleans med. surg. J.*, **100**, 510–517, May 1948. 18 refs.

1514. **Clinical Problems and Methods of Studying the Rh Factor for Gynaecologists.** (Klinische Probleme und Methodik zur Erfassung des Rh-Faktors für den Gynäkologen.)

By H. HOCKS. *Geburtsh. u. Frauenheilk.*, **8**, 438–449, May 1948.

1515. **Maternal Rh Sensitization and the Clinically Normal Child.**

By B. B. CARTER. *Amer. J. Obstet. Gynec.*, **54**, 879–882, Nov. 1947. 17 refs.

Since the Rh factor was first described it has been found difficult to account for the discrepancy

between the number of instances of Rh-negative mothers with Rh-positive children (1 out of 10 pregnancies) and the incidence of erythroblastosis foetalis (1 case in 200 deliveries). Four cases of maternal sensitization with no evidence of erythroblastosis foetalis in the child are presented. In all of them Rh agglutinins were demonstrable in the serum shortly after delivery and in 1 case some weeks before delivery. When the breast milk was tested it was found to contain Rh agglutinins. Although the babies were apparently healthy, Rh agglutinins could be demonstrated in 3 of them. Previous explanations, such as the inaccessibility of the maternal agglutinins to the baby's red cells or the immunity of the child's maternal red cells seem, therefore, unsatisfactory. *D. M. Stern*

1516. **Production of Anti-Rh Sera from Placental Tissue of Sensitized Women.**

By J. J. ENGELFRIED and F. R. HENRY. *Nav. med. Bull. Wash.*, **48**, 370–372, May–June 1948.

1517. **Death after Auto-transfusion.** (Todesfall nach Reinfusion.)

By E. E. MANUELIDIS. *Geburtsh. u. Frauenheilk.*, **8**, 431–438, May 1948. 1 fig., 27 refs.

1518. **Spontaneous Subarachnoid Haemorrhage in Pregnancy.** (Spontan subaraknoidalblodning ved graviditet.)

By H. RAMSTAD. *Nord. Med.*, **38**, 888–889, Apr. 30, 1948. 2 refs.

1519. **The Inter-relationship Between Pregnancy and Urinary Tract Disorders: with Case Report.**

By L. LAHN. *Urol. cutan. Rev.*, **52**, 140–144, Mar. 1948. 1 fig., 10 refs.

1520. **Pyelonephritis in Early Pregnancy.** (Pielonefritis precoz del embarazo.)

By C. E. DE LA COLINA and E. M. BALDI. *Obstet. Ginec. lat.-amer.*, **6**, 91–102, Mar.–Apr. 1948. 6 figs., 16 refs.

1521. **Uro-surgery in Relation to Pregnancy.**

By C. J. E. KICKHAM. *J. Urol.*, **59**, 953–959, May 1948. 6 refs.

1522. **Diabetes Insipidus and Uterine Atony. A Case Observed over a Period of 26 Years.**

By G. MARANÓN. *Brit. med. J.*, **2**, 769–771, Nov. 15, 1947. 12 refs.

The author describes a successful pregnancy in a patient with diabetes insipidus who had been observed over 26 years. The patient was first seen in 1921, aged 17; 4 months previously after sudden immersion in water at the seaside she began to complain of severe thirst and polyuria. Apart from irregular menstruation and reduction in the visual fields nothing of note was observed clinically. She was treated by injections of pituitrin which had to be stopped after the first ten because of dizziness and faintness. Five years later the condition was unchanged, but the patient had severe headache and was passing 20 litres of urine per day. There was an increase in size of the left breast and enlargement of the areola and nipple. New pituitary extracts were tried without effect. In 1933 the patient was delivered at term of a stillborn infant after 5 days without uterine contractions, labour never having properly started. She now had intense headache and projectile vomiting. In February, 1935, she had improved, and her urinary output was 7 litres per day. In October, 1935, she became pregnant again and the author advised pituitary extract on parturition. She was delivered of a living child. She was again pregnant in May 1936, but pituitrin was not available and labour pains ceased after the onset of labour. Three days later a dead foetus had to be removed. In April 1947 the patient was seen again, aged 43, living a normal life and now quite accustomed to her polyuria and thirst. A radiograph of the cranium was normal except for slight frontal hyperostosis.

The author describes his case as one of essential diabetes insipidus due to a disturbance of the hypothalamic-pituitary mechanism. The history of the sudden immersion suggests that the condition may have been due to a pathological prolongation of a normal physiological occurrence. He draws attention to the role of the posterior pituitary in the mechanism of parturition and compared the findings with those in animal experiments. He attributes the syndrome of uterine atony to a hypothalamic-posterior-pituitary insufficiency. A full bibliography of previous cases is given.

B. Sandler

1523. **An Investigation of Pregnancy in Diabetic Animals.** [In English.]

By G. HULTQUIST. *Acta path. microbiol. scand.*, **25**, 131–140, 1948. 3 figs.

1524. **General Infections of Pregnancy.**

By J. C. BROUNGHER. *Northw. Med., Seattle*, **47**, 356–358, May 1948. 11 refs.

1525. **The Estimation of Penicillin in the Amniotic Fluid, Foetal Blood, and the Maternal Blood.** (Stanovení penicilinu ve vodě plodové, v krvi pupečníkové a v krvi materske.)

By J. NOVÁK. *Ceskoslov. Gynaek.*, **12**, 422–432, 1947. 4 refs.

In order to ascertain the effect on the foetus of penicillin given to the mother antepartum, and its possible prophylactic value, the author determined penicillin levels in the amniotic fluid and foetal and maternal blood. The first 13 tests were carried out by the Oxford method, but as quantitative assessment was not possible by this technique, another was chosen. A series of decreasing concentrations of amniotic fluid and a foetal and maternal serum in physiological saline were mixed with a suspension of β-haemolytic streptococci in broth plus defibrinated blood of group O (1 in 100).

By this technique, which is described in detail, 64 tests were made, 30,000 units of penicillin being given to the mother by intramuscular injection at a time when delivery was expected within 2 hours. The results were grouped according to the interval after injection when delivery occurred. In the amniotic fluid, penicillin was found only in 6 cases in practically insignificant quantities. In the foetal and maternal blood, therapeutic levels were found 30 to 60 minutes after injection, lower levels before and after this period, and very low levels 90 to 140 minutes after injection. *A. Rohan*

1526. **Sulphonamide Metabolism in the Organism in Pregnancy and the Puerperium.** (Untersuchungen zur Frage des Sulfonamidstoffwechsels im Organismus der Schwangeren und Wöchnerinnen.)

By G. GAEHTGENS. *Z. Geburtsh. Gynäk.*, **128**, 225–247, 1947. 7 figs., 6 refs.

This article includes reports on the excretion rates of free and conjugated sulphonamides in women during pregnancy and the puerperium. [The total number of patients is not stated, but results are given for groups of 15 to 20 patients with each treatment.] Treatment consisted of the administration of "marfanil-prontalbin" alone, or the sulphonamide was given in conjunction with a vitamin preparation, vitamin B_1 or vitamin C. A greater proportion of acetylated sulphonamide was excreted by pregnant women than by non-pregnant women. The simultaneous administration of the water-soluble vitamin preparations led to an increase in the sulphonamide excretion and to a probable increase in the elimination of the amount of sulphonamide in a conjugated form. The authors point out that when increased amounts of the acetylated sulphonamide derivatives are excreted it is important to guard against urolithiasis, and they therefore recommend the administration of sodium bicarbonate and sodium citrate. Alternatively, only those sulphonamide preparations should be used which do not tend to produce crystalluria.

The results might be partly explained by the diuresis that occurs in pregnancy and by the hypovitaminosis which is commonly present during the puerperium. This is supported by the fact that in the normal healthy subject the administration of vitamin B_1 or vitamin C does not lead to an increase in sulphonamide excretion. However, the authors feel that attention should be drawn to the fact that in the treatment of infections after confinement the simultaneous administration of water-soluble vitamins with sulphonamides might lead to an increase both in the excretion of the sulphonamide and in the amount which is conjugated. *R. Wien*

1527. **Pulmonary Tuberculosis and Pregnancy.** (Lungentuberkulose und Schwangerschaft.)

By H. GOECKE. *Geburtsh. u. Frauenheilk.*, **8**, 423–431, May 1948. 39 refs.

1528. **The Placental Factor in Pathology of Pregnancy.** (El factor placentario en patologia gravídica.)

By P. NUBIOLA. *An. Med. Cirug.*, **23**, 234–240, Apr. 1948.

1529. **Effective Methods of Combating Intrauterine Foetal Asphyxia.** [In Russian.]

By A. P. NIKOLAEV and M. M. TYURINA. *Akush. Ginek.*, No. 1, 5–13, 1948.

1530. **Twin Pregnancy with Hydramnios of One Sac. (Contribution to Radiological Diagnosis.)** (Emarazo gemelar con polihidramnios de uno de los huevos. Contribución a su diagnóstico radiológico.)

By J. LEON. *An. brasil. Ginec.*, **13**, 183–188, Mar. 1948. 1 fig.

1531. **Combined Extrauterine and Intrauterine Pregnancy.**

By J. O. RUDE. *Northw. Med., Seattle*, **47**, 358, May 1948.

1532. **Extrauterine Pregnancy.** (Uber extrauteringraviditäten.)

By H. HEBERER. *Geburtsh. u. Frauenheilk.*, **8**, 397–400, Apr. 1948.

1533. **Seven Months' Extrauterine Abdominal Pregnancy.** (Embarazo extrauterino abdominal de 7 meses: presentación de un caso clínico.)

By L. BENAVIDES. *Ginec. Obstet. Mexico*, **3**, 129–138, Mar.–Apr. 1948. 3 figs.

1534. **Double Ectopic Pregnancy in One Tube.** [In English.]

By D. TROLLE. *Acta obstet. gynec. scand.*, **27**, 395–401, 1948. 9 refs.

1535. **Tubo-ovarian Pregnancy in a Tuberculous Tubo-ovarian Cyst.** (Grossesse tubo-ovarienne dans un kyste tubo-ovarien tuberculeux.)

By P. BURGER. *Rev. franç. Gynéc.*, **43**, 126–132, Apr. 1948.

LABOUR

1536. **Variations in Pulse and Arterial Blood Pressure During Uterine Contraction and their Relations to Myocardial Function.** (Le variazioni del polso e della pressione arteriosa durante la contrazione uterina nei loro rapporti con la funzione miocardica.)

By A. PAVONI. *Mon. ostet.-ginec.*, **18**, 281–305, July–Dec. 1947. 6 figs., 33 refs.

These investigations, carried out on 94 women in labour at the School of Obstetrics in Udine, are based on the consideration that a uterine contraction: (*a*) results in a reduction of the vascular surface area of the body and in the transfer of a larger amount of blood into the general circulation; (*b*) constitutes work; and (*c*) being painful, stimulates the vegetative nervous system.

During periods extending over four to five uterine contractions in the first stage of labour the pulse

rate was registered for 15 seconds at intervals of 15 seconds, and the systolic and diastolic blood pressures were recorded at similar intervals. The patient's general condition, cardiac abnormality (if any), the dilatation of the uterine os, and the strength and duration of the uterine contractions were also noted. The author distinguishes between four types of results: (1) Normal. Just after the onset of a uterine contraction the pulse rate rises rapidly but soon gradually returns to normal. This coincides with an increase in the systolic blood pressure. The rise in blood pressure is in proportion to that of the pulse rate, and the extent of both depends on the intensity and duration of the uterine contraction. (2) Slight functional impairment. The rise in blood pressure and pulse rate is normal, and so is the relation between the two. The decrease in the pulse rate, however, is delayed. (3) Moderate impairment. There is a normal rise and fall in pulse rate. The rise in blood pressure, however, is delayed in its onset and reaches its maximum towards the end of, or even after, the uterine contraction. (4) Considerable impairment. This type is characterized by obvious disproportion between pulse rate and blood pressure. The former rises during a uterine contraction to heights quite out of proportion to the latter. There may also be an association with types (2) and (3). The author admits that in these investigations the problem has been approached from the point of view of haemodynamics and the functional state of the cardiac muscle only, and that extracardiac factors—constitutional, endocrine, and neuro-vegative—may influence the results. ***N. Alders***

1537. **Critical Observation of Wolf's Concept of the Mechanics of Labour.** (Kritische Betrachtungen zu W. Wolfs Geburtsmechanik.)

By G. DODERLEIN and G. KLUMBIES. *Zbl. Gynäk.*, **69**, 945–958, 1947. 4 figs., 11 refs.

1538. **Roentgenographic Visualization of the Placenta in the Third Stage of Labor. A Preliminary Report.**

By D. ROBINSON and W. S. BOYD. *Amer. J. Roentgenol.*, **58**, 730–732, Dec. 1947. 1 fig., 12 refs.

The authors briefly review methods of placental visualization, and describe a technique for placental radiography in the third stage of labour. Amniography is mentioned and its dangers are stressed [it is curious that no reference is made to the danger of inducing premature labour]; cystography and soft-tissue radiography are briefly described, and there is a note on a series of 5 cases in which the placenta was accurately located by tomography. For the technique described the patient is delivered on a urological X-ray table and 20 ml. of " diodrast " is used as an opaque medium. The syringe is ready filled and the needle inserted into the umbilical artery as soon as the infant is born. When the operator is certain that the needle is in the artery the cord is severed and the diodrast injected. Only one placentogram is shown, taken 1 minute after the injection, but the text states that further exposures are made at 3 and 5 minutes. There were no ill effects, and it is claimed that this method will aid in the diagnosis of placenta accreta and will increase knowledge of placentation. The X-ray factors quoted are 77.8 kV (peak), 15 mA, 2 seconds exposure, and 30-in. (75-cm.) target-film distance. *Hugh R. Arthur*

1539. **The Immediate Postpartum Period as a Fourth Stage of Labor.**

By C. T. JAVERT. *Amer. J. Obstet. Gynec.*, **54**, 1028–1032, Dec. 1947. 14 refs.

The author defines the fourth stage of labour as the interval from the expression of the placenta until complete reaction of the patient to the delivery, including a satisfactory contraction of the uterus without excessive bleeding. Its duration varies from the traditional hour to many hours if abnormal events occur. Twenty-eight of the 88 maternal deaths that occurred in the New York Lying-in Hospital from 1932 to 1945 took place during the fourth stage and were due to such causes as postpartum haemorrhage, cerebrovascular accidents, cardiac failure, anaesthesia, aspiration pneumonia, rupture of the uterus, and transfusion reactions. The clinical, anatomical, physiological, and pathological characters of the fourth stage are described. The events occurring in it should be recorded as a part of the history of labour, for it is truly a part of labour. *F. J. Browne*

1540. **Medical Method of Assisting Normal Labour.** (Méthode d'accouchement médical.)

By A. BADESCO. *Presse méd.*, **55**, 780–781, Nov. 15, 1947.

A method of assisting normal labour is described. It consists in the intramuscular administration of methylene blue; 150 mg. in 3 per cent solution (freshly prepared and tyndallized at 60°C.) is injected during the first stage of labour when dilatation has reached 1 to 2 cm. The membranes are ruptured simultaneously, if the periods of rest between the pains are less than 2 minutes or if the pains are irregular in duration or intensity. In addition " pantopon " (papaveretum) is administered subcutaneously if uterine relaxation between pains is not complete. If the labour is not completed within 2 hours of the injection a further 100 mg. is administered. Of primiparae 23 per cent in 2 to 3 hours after injection, 46 per cent in 3 to 4 hours, and 8 per cent in 5 hours or more after injection (in the author's opinion delay in this last group is due to administering methylene blue too late). The author concludes that this is a valuable auxiliary measure in normal labour, especially in primiparae, when it is certain that there is no disproportion. The total duration of labour is materially shortened in all cases, and no deleterious after-effects either on the mother or on the baby have been noted. *Nicolas Tereshchenko*

1541. **A New Method of Surgical Induction of Labour.** (Nová metoda vyvolání porodních bolestí.)

By A. LEWI. *Ceskoslov. Gynaek.*, **12**, 478–482, 1947.

In cases in which labour has to be induced prematurely (thirty-second to thirty-sixth week) for reasons such as toxaemia, heart disease, pelvic contraction, the usual methods of medical and surgical induction often fail. In such cases (after artificial rupture of membranes and sometimes, if necessary, slight dilatation of the cervix) the author applies Willett's scalp-traction-forceps and attaches a weight of 300 to 500 g. This method brings on labour within 4 to 8 hours. The author has not observed any foetal or neonatal deaths or maternal complications attributable to this method [he does not, however, give any figures]. *A. Rohan*

1542. **Induction of Premature Labour.** (Parto prematuro artificial.)

By L. ALONSO-BUENA POSADA. *Toko-ginec. pract.*, **7**, 150–172, Apr. 1948. 35 refs.

1543. **The Significance of Cervical Dilatation in Trial Labour in Breech Presentations with Contracted Pelvis.** (L'épreuve du travail sur le col au cours des accouchements en présentation du siège dans les bassins rétrécis.)

By —. RIVIÈRE, —. CHASTRUSSE, and —. MISSON. *Rev. franç. Gynéc.*, **42**, 303–310, Nov. 1947.

In discussing breech delivery in the presence of contraction of the pelvis, the authors emphasize the importance of the rate of dilatation of the cervix in prognosis. The behaviour of the cervix during labour is the best indication of the function of the uterus as a whole. Slow dilatation is an indication of poor action of the uterine muscle and thus a sign of dystocia. On the other hand, rapid dilatation is accompanied by powerful rhythmic contractions and a good outlook for spontaneous delivery.

This clinical study is based on 45 cases of breech presentation with contracted pelvis collected over 10 years from 1936 to 1945. From 1936 to 1942 Caesarean section was the rule and was performed in 15 cases out of 23. In all but 1 of these 15 cases the infant did well. The 1 foetal death was accounted for by multiple malformations. The 8 deliveries by the natural passages resulted in 1 foetal death due to cerebral haemorrhage after a difficult forceps delivery of the after-coming head. In 1943 and 1944 the patients were allowed to go into labour spontaneously. The course of labour was studied with particular reference to the rate of dilatation of the cervix. Of 16 cases, 9 ended in spontaneous delivery, 3 in extraction of the breech, and 4 in Caesarean section. In 1 of the cases in which extraction was performed, foetal death from cerebral haemorrhage resulted. In 1945 posterior pituitary extract was used when necessary to stimulate the uterus. In 1 case manual dilatation of the cervix and bringing down a leg resulted in successful delivery. The authors believe that the behaviour of the cervix during labour should enable the obstetrician to decide when Caesarean section should be performed and when spontaneous delivery can be anticipated. [It is generally held that " trial labour " cannot be conducted in the presence of breech presentation, since the very essence of trial labour is that it is a test of the ability of the foetal head to pass through the maternal pelvis. Few obstetricians in Britain would embark on breech delivery in the presence of contracted pelvis unless the child was obviously small. This article would be more convincing if the observations had been reinforced by X-ray measurements of the pelvis. It appears also that no attempt at external version had been made in any of the cases described.]

Josephine Barnes

1544. **The Effect of Thiamine Hydrochloride on the First and Second Stages of Labour.** (El clorhidrato de tiamina y sus efectos en los períodos de dilatación y expulsion del parto.)

By J. H. DUBIAU, O. TIMMERMANN, and L. GEISSE. *Rev. méd. Chile*, **75**, 672–673, Oct. 1947.

The authors report the results in 21 patients of an intramuscular injection of 30 mg. of thiamine hydrochloride at the beginning of the first stage of labour, together with a similar dose at the beginning of the second stage. All patients had normal, or only slightly contracted, pelves. No other drugs were used. In 10 primigravidae the first stage averaged 6 hours 33 minutes and the second stage 40 minutes. [No control figures are given.] Forceps were used in 2 patients with small pelves and large babies. In another patient with a small pelvis manual dilatation of the cervix and internal version and extraction were carried out. In yet another patient a prolapsed cord was replaced and an oxytocic given. In 11 multigravidae with normal pelves the first stage averaged 4 hours 12 minutes and the second stage 11½ minutes. In 1 patient who refused the second injection the second stage lasted 75 minutes, and in another an oxytocic was required for a third stage lasting 30 minutes.

The authors believe that this drug shortens the first and second stages, and that there is less pain than usual and in some cases marked sleepiness. Uterine contractions are more powerful and regular, oxytocics are unnecessary, and no harmful effect on mother or baby has been found.

Bryan Williams

1545. **Electric or Electro-drug Technique in Labour.** (A propos de l'accouchement électrique ou électro-médicamenteux.)

By C. LEVASSEUR, M. NORDMANN, and M. CHAPPUIS. *Gynécologie*, **44**, 177–208, July–Aug., 1947. 18 figs.

The authors describe the use of a sinusoidal electric current with the object of accelerating the course of labour. Patients chosen were in normal

labour, or labour capable of being made normal, with the presenting part engaged. Treatment was begun when the cervix was about 4 cm. dilated in primiparae and about 2 cm. dilated in multiparae. In addition an injection of " solution 5 " (1 unit of posterior pituitary extract, 20 mg. of opium extract, 30 mg. phenobarbitone) or of " solution 12 " (1 unit of posterior pituitary extract, 1 g. magnesium hyposulphite, 10 mg. " eucodal ") was given. An attempt was made to dissociate the action of the three and the results are given under four headings: (1) Twelve observations where electricity was used without injection of either solution, or artificial rupture of the membranes. (2) Five observations after injection of " solution 12 ". (3) Four observations after injection of " solution 5 ". (4) Four observations in which, after psychological preparation of the patient, the electrical apparatus was applied without turning on the current. Two methods of study were used. Uterine contractions were recorded by the utero-tensometer. The " curve of dilatation " of Vignes and Breil was plotted to observe the effect on the rate of dilatation of the cervix. The results from the use of electricity alone showed that in 6 dilatation appeared to be accelerated. In 1 case the normal course of labour was accelerated, while in another it appeared to be retarded. The authors conclude that patients exhibit an individual sensitivity to the effect of the electric current. The general conclusion is that the solutions were more effective than the electric current. The best results were obtained by a combination of electricity and injections. The value of psychological suggestion is stressed.

[The small number of observations in each of the four groups makes the value of these doubtful, since it is well known how variable the course of labour may be even in normal women. It is interesting to note that a good effect was obtained when the electrical apparatus was used without turning on the current.] *Josephine Barnes*

1546. **Leading Considerations in the Problem of Active or Conservative Management of Labour.** (Wytyczne uwagi w sprawie czynnego i zachowawezego postepowania w czasie porodu.)

By K. BOCHENSKI. *Przeg. Lek.*, **3**, 756–762, Nov. 1947.

1547. **Spontaneous Rupture of the Uterus During Dystocia Due to Fibroid in Pelvis.** (Rotura espontánea del utero y vejiga en parto distócico por fibroma uterino previo.)

By F. PEREZ ACOSTA. *Rev. méd.-quirurg. Oriente*, **9**, 10–18, Mar. 1948. 2 figs., 5 refs.

1548. **Dystocia and Monsters.** (Distocias y monstruos.)

By F. M. FERRER. *Rev. esp. Obstet. Ginec.*, **7**, 93–102, Mar.–Apr. 1948. 2 figs.

1549. **The Course of Labour in Congenital Dislocation of the Hip.** (Geburtsverlauf bei angeborener Hüftgelenksluxation.)

By F. RENDELSTEIN. *Klin. Med. Wien.*, **3**, 293–297, Apr. 15, 1948. 3 refs.

1550. **Abnormal Presentation.**

By H. H. WARE. *J. Amer. med. Ass.*, **137**, 448–450, May 29, 1948. 5 refs.

1551. **Shoulder Delivery in Cephalic Presentation.** (Skulderløsning ved hodefødsel.)

By J. LØVSET. *Nord. Med.*, **38**, 1127–1128, June 4, 1948. 1 fig.

1552. **Prognosis in Breech Delivery with Special Reference to Application of Forceps to the Breech.** (Sulla prognosi ed il trattamento del parto podalico con particolare riguardo alla varieta' natiche e all'applicazione del forcipe sul podice.)

By NIOSI-CUSIMANO. *Mon. ostet.-ginec.*, **18**, 169–189, July–Dec. 1947. 41 refs.

The author reports on 146 breech deliveries at the Obstetrical and Gynaecological Clinic of the University of Pisa. In 59 cases (40.4 per cent) surgical intervention proved necessary. In 13 cases Kielland's forceps was applied to the presenting breech without foetal mortality or serious maternal morbidity. The indications for intervention were foetal distress, uterine inertia, and maternal eclampsia.

[The (corrected) foetal mortality in the author's series of breech deliveries is 6.6 per cent—that is, 1 in 16. A foetal mortality of nil in his 13 cases of breech delivery by forceps is, therefore, statistically insignificant. While this method has had its place in operative obstetrics, ever since Levret applied the forceps to a breech, mistaking it for the head, almost 200 years ago, it is not likely to alter materially the foetal mortality in breech deliveries, since the really dangerous procedure is delivery of the head.] *N. Alders*

1553. **Opisthotonos Fetalis in Breech Presentation. Report of a Case with Bilateral Congenital Posterior Dislocation of the Tibiae.**

By G. F. MELODY. *Calif. Med.*, **68**, 378–380, May 1948. 4 figs., 12 refs.

1554. **Face Presentation.**

By S. J. RUDOLPH. *Amer. J. Obstet. Gynec.*, **54**, 987–993, Dec. 1947. 1 fig., 1 refs.

At the Philadelphia Lying-in Hospital there were 61 face presentations in 35,163 deliveries—that is, 1 in 576. Faulty position of the uterine axis, usually given as a cause, was not blamed in any of the cases. The malpresentation was about equally common in primiparae and multiparae. In 11 of the 29 primiparae and 7 of the 32 multiparae some form of pelvic abnormality was present. Twenty-five of the infants were over 8 lb. (3.6 kg.) in weight, and in almost half the cases there was

disproportion, either due to contracted pelvis or to the size of the child. In one case the cord was three times round the foetal neck. Seven infants (11 per cent) were monsters—5 anencephalics and 2 cases of acraniorachischisis. There was only 1 case of placenta praevia. There were no maternal deaths, but the foetal and neonatal mortality (19.7 per cent) was nearly 4 times the average for the hospital. This, however, included the 7 monsters and an infant weighing under 2 lb. (0.9 kg.).

According to the textbooks the incidence of the various positions in cases of face presentation is closely correlated with the incidence of the vertex position, to which they correspond—that is, 85 per cent right mento-posterior and left mento-anterior. In this series, however, there was an almost equal distribution between left and right mento-anterior and left mento-posterior positions. A right mento-posterior position occurred only 4 times. Of the mothers 19 were delivered spontaneously, and 16 were delivered by forceps without rotation. Internal podalic version was required in 14 cases, and Caesarean section in 8. Rotation and forceps delivery were necessary in 4. The duration of labour for both primiparae and multiparae was far below the average. The author concludes that the majority of patients in cases of face presentation can be safely delivered spontaneously or by low forceps, while Caesarean section is safest if there is disproportion. *F. J. Browne*

1555. **Manual Removal of the Placenta.**

By R. W. DEVOE and A. B. HUNT. *West. J. Surg. Obstet. Gynec.*, **55**, 647–650, Dec. 1947. 5 refs.

Manual removal of the placenta has always been attended by considerable risk. In 1928 a mortality rate of 10 per cent was recorded by Bumm, and in 1937 a corrected mortality rate of 2.6 per cent with a morbidity rate of 31.5 per cent was recorded by Block. In recent years both mortality and morbidity rates have been considerably lowered by increasing care in asepsis and by chemotherapy. The present study is based upon the results of the procedure carried out in 98 of the 6,753 obstetric patients treated at the Mayo Clinic between the years 1936 and 1945. The usual technique was employed in all cases; in 70 per cent the uterine cavity was subsequently packed with gauze. One patient died, and the morbidity rate in cases where the operation was performed early was 4.4 per cent. In 9 cases of the series, optimal conditions were not present and the morbidity rate rose to 7.7 per cent. The authors hold strongly that manual removal of the placenta, performed under the best conditions, should not be carried out only as a last resort in the treatment of postpartum haemorrhage. They believe, with Pastore, that the early and proper use of the method in cases of progressive postpartum haemorrhage will reduce the incidence of postpartum complications. Moreover, the procedure is indicated in cases not associated with excessive blood loss, in which the placenta has been retained for at least an hour after the expulsion of the infant. *Falkland L. Cary*

1556. **The Aetiology, Prevention and Treatment of Retained Placenta.**

By K. M. D. HARDING. *Med. Press*, **219**, 457–458, May 26, 1948.

1557. **Spontaneous Formation of a Haematoma during Labour.** (Spontanhämatombildung unter der Geburt.)

By R. GERLACH. *Zbl. Gynäk.*, **69**, 973–974, 1947.

1558. **"Pervitin" ("Methedrine") Treatment of Intrauterine Asphyxia.** (Die Pervitintherapie der intrauterinen Asphyxie.)

By A. ROCKENSCHAUB. *Wien. klin. Wschr.*, **59**, 797–799, Dec. 5, 1947. 2 figs., 15 refs.

The author points out that impending intrauterine asphyxia is often the reason for intervention during labour, and that until 1941 the only method of saving the foetus was by application of forceps if the cervix was fully dilated or by Caesarean section if asphyxia occurred early in labour. In 1941 Nevinny recommended the intravenous injection of "cardiazol" (leptazol) and Froewin a little later suggested the use of "pervitin" ("methedrine") by mouth, the idea being to improve the circulation and tone of the heart muscle and hence increase the rate of blood flow in, and absorption of oxygen from, the placenta. Statistics are given for three groups of cases. (1) Untreated: 56 cases of intrauterine asphyxia; 8 infants were not asphyxiated at birth while 48 were asphyxiated (28 being dead). (2) Treated with cardiazol: 46 cases of impending asphyxia were treated, and 24 infants were born asphyxiated, 11 being dead. (3) Treated with methedrine: 62 cases; only 11 infants were born asphyxiated, 4 being dead. In all groups it will be noted that one-half of the foetuses born asphyxiated were dead. The cause of death in the majority was a tentorial tear or aspiration of liquor amnii. The frequency of forceps delivery for foetal distress was reduced considerably—with cardiazol treatment it was only 45 per cent of the previous rate and with methedrine treatment only 18 per cent. *Gladys Dodds*

1559. **Fatal Obstetric Shock and Phaeochromocytoma.** (Choc obstètrical mortel et paragangliome hypertensif de la surrénale.)

By L. DIGONNET, J. THOYER-ROZAT, B. DUPERRAT. *Gynéc. et Obstét.*, **46**, 677–682, 1947. 2 figs., 5 refs.

A description is given of a case of fatal obstetric shock due to an associated phaeochromocytoma (chromaffinoma, paraganglioma) of the right suprarenal. The patient, a 3-gravida, had typical attacks of intermittent hypertension during her second pregnancy. When seen during her third

and last pregnancy she had persistent hypertension without albuminuria or oedema. The patient became gravely shocked 2½ hours after spontaneous delivery. This state of shock responded to treatment but recurred after 36 hours and proved fatal. At necropsy, a phaeochromocytoma of the right suprarenal was found with considerable haemorrhagic necrosis of the tumour substance. All other organs, including the kidneys, pituitary, and placenta showed no pathological change. The author suggests that the necrosis of the tumour may have some bearing on the production of shock.

D. M. Sheppard

ANAESTHESIA

1560. **Analgesia and Anaesthesia in Obstetrics.** (Analgésie et anesthésie obstétricales.)

By F. DE SENARCLENS. *Praxis*, **37**, 306–308, Apr. 29, 1948.

1561. **Combined General and Local Anesthesia for Vaginal Delivery.**

By E. A. GRABER and S. DRUCE. *N.Y. St. J. Med.*, **48**, 1269–1270, June 1, 1948. 4 refs.

1562. **Nitrous Oxide Anaesthesia in Gynaecology and Obstetrics.** (Uber die Stickoxydulnarkose in der Gynäkologie und Geburtshilfe.)

By G. IMHOLZ. *Geburtsh. u. Frauenheilk.*, **8**, 385–396, Apr. 1948. Bibliography.

1563. **Sodium Pentothal Anesthesia for Selected Vaginal Obstetrics.**

By A. L. DIPPEL, R. J. HELMAN, C. E. WOLTERS, H. A. WALL and F. H. HAIRSTON. *Surg. Gynec. Obstet.*, **85**, 572–582, Nov. 1947. 13 refs.

In the division of obstetrics at the Hermann Hospital, Texas, intravenous "sodium pentothal" anaesthesia was introduced in the 1939–45 war because of the shortage of anaesthetists for routine work. Before this all deliveries had been effected with perineal block analgesia. The properties and action of sodium pentothal are described, and it is stated that this drug passes rapidly into the foetal circulation and reaches equal concentration in foetal and maternal blood in 10 to 12 minutes. Pentothal has a markedly depressant effect on the respirations of the baby. Maternal contraindications to the use of pentothal are heart disease and the possibility of respiratory obstruction. Toxaemia should be a contraindication, but no adverse effects were observed in that condition. Between July 1945, and October 1946, 350 patients were delivered under pentothal anaesthesia. Administration of the drug began only when a rapid delivery was anticipated. A 2 per cent solution of sodium pentothal was injected slowly until the patient stopped counting, when a further 5 ml. of solution was given. Further amounts were injected if the patient showed evidence of wakening. The cord was clamped immediately after delivery to avoid further transference of the drug to the baby. Pentothal did not affect the uterine action, and there was no increase in blood loss. In 89.5 per cent of cases no special resuscitative measures were required for the baby, but in 10.5 per cent resuscitation was necessary. The authors conclude that sodium pentothal anaesthesia, while carrying no special advantages, when used carefully carries no special risk for the mother or baby. Many tables of statistics are given referring to this group of patients.

[This article contains a bewildering mass of statistics (17 tables in all). It is difficult to draw any conclusions; the practice of obstetrics at this centre is different from that in Britain in that every patient appears to have complete anaesthesia for delivery and the forceps rate is extremely high.]

L. W. Lauste

1564. **Sodium Pentothal Anesthesia in Obstetrics.**

By C. L. COOLEY and H. F. SCHWARZ. *West J. Surg. Obstet. Gynec.*, **56**, 278–284, May 1948. 3 refs.

1565. **Low Spinal Nupercaine Anesthesia in Obstetrics.**

By H. E. SCHMITZ and G. BARA. *Amer. J. Obstet. Gynec.*, **54**, 838–847, Nov. 1947. 12 refs.

Before administration of "nupercaine" every patient was tested for sensitivity. Perineal analgesia usually lasted for more than 3 hours; where longer analgesia was desired more than one dose was given. Injection was given late in the first stage or early in the second stage of labour, the dose being up to 2 ml. of a 5 per cent glucose solution containing 2.5 per cent nupercaine per ml. Some untoward effects occurred—fall in blood pressure, foetal bradycardia, and headache. The following is the authors' table of results:

Total number of low spinal cases ...		375
Total number with complete subjective relief for at least 1 hour		359
Cases with complete relief with one injection	328	
Cases with complete relief with two injections	31	
Cases with complete relief after each of two injections ...	23	
Cases with incomplete relief with first but complete after second injection	5	
Cases with complete relief with first but incomplete with second injection	3	
Total number of incomplete relief cases		13
Cases with incomplete relief after one injection	12	
Cases with incomplete relief after each of two injections ...	1	
Total number of complete failures ...		3

D. M. Stern

PUERPERIUM

1566. **The Physiological Maternal Blood Picture in the Puerperium.** (Das physiologische mütterliche Blutbild im Wochenbett.)

By —. ARNETH. *Zbl. Gynäk.*, **69**, 974–977, 1947. 9 refs.

1567. **Advantages of Early Ambulation after Confinement.** (Les avantages du lever précoce après l'accouchement.)

By R. KELLER and A. GINGLINGER. *Gynéc. et Obstét.*, **47**, 310–312, 1948.

1568. **Classification of Puerperal Disease.** [In Russian.]

By S. B. RAFALKES. *Akush. Ginek.*, No. 1, 43–47, 1948.

1569. **The Problem of Rational Classification of Puerperal Disease.** [In Russian.]

By A. V. BARTELS. *Akush. Ginek.*, No. 1, 47–54, 1948.

1570. **The Causative Organisms of Puerperal Infections and their Specific Therapy.** (Uber die Erreger puerperaler Infektionen und deren kausale Therapie.)

By P. BERNHARD. *Zbl. Gynäk.*, **69**, 882–897, 1947. 19 refs.

Bacteriological examination revealed anaerobic pathogens in 52 of 104 women suffering from puerperal infection. Gas-gangrene organisms were found in 46.2 per cent of cases and anaerobic streptococci in 6.7 per cent. In only 8.6 per cent of all cases was infection due to a single organism, while in 91.4 per cent there were mixed infections with 2 to 7 different organisms. Since efficient chemotherapeutic agents must act on both aerobic and anaerobic bacteria, the author considers the combinations "de-ma" ("debenal" or sulphadiazine with "marbadal", which is a "marfanil" derivative) and "supronal" (sulphamerazine with marbadal) to be more suitable for the treatment of puerperal infections. The mixture de-ma has given the best results to date. *Harold Jarvis*

1571. **The Conquest of Puerperal Infection 1846–1946.**

By E. S. BRACKETT. *Rhode Island med. J.*, **31**, 235–239 and 246, Apr. 1948.

1572. **Uterine Gangrene Among 7,500 Deliveries.** (Gangrena uterina.)

By R. PUMARINO. *Bol. trim. Hosp. Vina d. Mar.*, **4**, 41–44, Apr. 1948. 3 refs.

1573. **Anaerobic Micro-organisms in Puerperal Infection.** [In Russian.]

By S. G. YUREVSKI. *Akush. Ginek.*, No. 1, 32–35, 1948.

1574. **Penicillin and Pregnancy.** (Pénicilline et grossèsse.)

By A. KHOURY. *C. R. Soc. franç. Gynéc.*, **18**, 86–88, Mar. 1948. 2 refs.

1575. **Use of Penicillin in the Treatment of Puerperal Infection.** [In Russian.]

By E. A. MOGNYAN. *Akush. Ginek.*, No. 1, 37–38, 1948.

1576. **Penicillin Treatment of Retained Placental Fragments in the Late Puerperium.** (Penicillinbehandlung bei Plazentaresten in Spätwochenbett.)

By H. TISCHER. *Klin. Med., Wien*, **3**, 309–316, Apr. 15, 1948. 3 figs., 13 refs.

1577. **Application of Penicillin Therapy in Obstetrics and Gynaecology.** [In Russian.]

By I. I. ZEMLINSKAYA. *Akush. Ginek.*, No. 1, 39–40, 1948.

1578. **Puerperium Complicated by Uterine Tumour.** (Un caso de puerperio complicado por tumor uterino.)

By R. HORNO LIRIA. *Rev. esp. Obstet. Ginec.*, **7**, 107–112, Mar.–Apr. 1948. 2 figs., 5 refs.

1579. **Postpartum Eclampsia Supervening Later than Three Days after Delivery.**

By H. ACOSTA-SISON. *J. Philippine med. Ass.*, **24**, 115–117, Mar. 1948. 1 ref.

LACTATION

1580. **Lactation in the Light of the Latest Investigations.** (Wydzielanie mleka w świetle najnowszych badan.)

By A. KELHOFFER. *Przeg. Lek.*, **3**, 532–536, Aug. 15, 1947.

The literature on recent investigations into hormonal and neuropsychic factors in lactation is reviewed. The author describes his own experience in the treatment of 24 cases of failure of lactation with "suppletan". Suppletan was first manufactured as an ointment for local application and contained prolactin (100 pigeon units in 20 g.), oestrone, cod-liver oil, "vaseline", and "lanolin". Recently, however, it has been produced as a suppository and it was in this form that the author employed it. The treatment failed when it was started on the sixth day or later. One suppository was used twice daily for a period of 5 days. In 2 cases there was no response; in the others the breasts again became congested and there was a three-fold to four-fold increase in milk yield. In 2 cases this increase was maintained; in the rest the milk yield fell but remained twice as high as it was before treatment. *C. Uhma*

1581. **Effects of Gonadotrophic Hormones on Lactation.**

By G. M. C. MASSON. *Proc. Soc. exp. Biol., N.Y.*, **66**, 506–508, Dec. 1947. 1 fig., 15 refs.

The inhibiting effect of steroids on lactation is mediated through the ovaries and is probably due to the hormonal secretions of the large corpora lutea formed under the influence of the steroids. Since the ovaries are normally stimulated by

gonadotrophins of pituitary or chorionic origin, it was decided to investigate the effect of these hormones on lactating rats. Similar groups of albino rats with 6 young in each litter were studied from the day after parturition until necropsy, which was performed on the seventeenth day or earlier if all the litter died. Criteria of efficiency of lactation were provided by the growth curves of sucklings and by the number of deaths among the young. Mammary glands and genitalia were carefully investigated histologically after death. The influence of anterior pituitary preparations and of varying dosage of chorionic gonadotrophin and pregnant mare serum was studied. Pregnant mare serum strongly inhibited lactation and caused the death of most of the young. Chorionic gonadotrophin had a slight effect on the growth curve of the young, while an anterior pituitary preparation was inactive. From histological studies of the ovary, vagina, and uterus, it is suggested that the activity of pregnant mare serum is due to a high level of oestrogens and progesterone.

Doreen Daley

THE INFANT

1582. **The Physiological Loss of Weight in the Newborn Infant and an Attempt at the Prevention of this Loss.** (Fysiologicky úbytek váhovy u novorozencu a vliv prevence tohoto váhového spádu.)

By J. STRUMA. *Ceskoslov. Gynaek.*, **12**, 411–422, 1947. 1 fig.

All babies born in 1946 at the Second Obstetric Clinic of Prague University received 3-hourly during the first 24 hours (starting 12 hours after birth) 15 to 20 g. of fluid consisting of equal parts of Ringer's solution and sweetened tea. The initial weight loss of these babies was compared with that of all babies born in 1945, when no special precautions had been taken. The author found that there was no significant difference in favour of the 1946 group; babies whose initial weight was low lost significantly more weight under the special regime. It is concluded that the initial weight loss is, in fact, physiological, and special measures to prevent it are unnecessary and futile. Any loss beyond the physiological maximum of 10 per cent, however, must be combated. *A. Hohan*

1583. **Physiological Oedema of the Newborn.** (Edema fisiológico del recién nacido.)

By R. ORTHEGA and O. JIMENEZ. *Rev. chil. Pediat.*, **18**, 843–854, Nov. 1947. 3 figs., 14 refs.

1584. **The Coronary Arteries of Infants.**

By W. L. MINKOWSKI. *Amer. J. med. Sci.*, **214**, 623–629, Dec. 1947. 1 fig., 21 refs.

The author, at the Beth Israel Hospital, New York, examined histologically sections of coronary arteries of 122 male and 82 female infants. The vast majority were stillborn or less than one week old. The literature is reviewed, with particular reference to the investigations of Dock (*J. Amer. med. Ass.*, 1946, **131**, 875). Intimal changes, such as the presence of a musculo-elastic and/or elastic layer, were found in 60 per cent of male and 51 per cent of female infants.

To study the influence of sex on these coronary changes the author selected a group of 51 males and 25 females not more than 1 day old in whom the cause of death was either birth injury or asphyxia. He estimated the intima : media ratio of the coronary arteries, and found that the mean difference between male and female was significant. Of the male infants 43 per cent showed varying degrees of intimal thickening compared with 35 per cent of females. Intimal changes were found often in older infants and children in whom death had followed bronchopneumonia or other infection. Whatever the significance of the sex difference in thickness of coronary intima and whatever the importance of bacterial or other toxins in the production of these changes, the true meaning of their findings and their relation to adult atherosclerosis and the so-called early adult arteriosclerotic lesion, constitute, according to the author, still unsolved problems. *A. I. Suchett-Kaye*

1585. **Glomerular Filtration Rate, Effective Renal Blood Flow, and Maximal Tubular Excretory Capacity in Infancy.**

By J. R. WEST, H. W. SMITH, and H. CHASIS. *J. Pediat.*, **32**, 10–18, Jan. 1948. 4 figs., 17 refs.

The authors, at the New York University College of Medicine, discuss the development of glomerular and tubular function in children up to 2 years of age, renal function being correlated with body surface area.

In 23 normal infants estimations were made, by the methods described by Goldring and Chasis for adults, of: (1) mannitol clearance (rate of glomerular filtration), (2) *p*-aminohippurate clearance (effective renal plasma flow), and (3) maximal tubular excretory capacity for *p*-aminohippurate. Both substances were administered in doses varying with body weight to give suitable plasma concentrations in an intravenous normal saline infusion (250 ml. at 2 to 4 ml. per minute), with a second dose of *p*-aminohippurate after 30 minutes. After a further 30 minutes urine was collected by catheterization, the bladder being washed out with sterile saline after each collection. In later tests the mannitol was determined by the chromotropic-acid method of Corcoran and Page.

The authors found that the filtration rate increases from 3 ml. per minute in the first week of life to 40 to 50 ml. per minute at 1 year. From their data the correlation between renal function and body surface area appears to exist at ages under 2 years, the adult filtration rate of 124 ml. per 1.73 sq. meters being reached in some infants at the age of 10 to 20 weeks. The renal plasma flow

increased from 12 ml. per minute in the first week to 140 ml. per minute at 1 year. The adult mean (646 ml. per 1.73 sq. metres) was reached by 30 weeks in some cases. The maximal tubular excretion of *p*-aminohippurate increases from 2.6 mg. a minute to 25 mg. a minute, and reaches the adult value at 30 weeks (77.5 mg. a minute per 1.73 sq. metres). It is concluded that these three functions are adjusted before the age of 1 year to the metabolic requirements of the body, for which the surface area is taken as an index, but that in early infancy the adjustments take place at different rates. Examination of the various ratios shows: (1) A proportional increase in renal blood flow with the development of the renal tubules. (2) A high filtration fraction in early months, due either to imbalance between glomerular and tubular development or to a low extraction ratio in the blood perfusing the tubules—a point which requires further study. The authors suggest that the preponderance of glomerular function over tubular function may be due to the large glomerular surface and increased pressure found in the infant kidney. *Morag L. Insley*

1586. **Cardiac Murmurs in Infancy.**

By N. Cox. *Brit. med. J.*, **1**, 148–150, Jan. 24, 1948. 7 refs.

In a preliminary report on the significance of cardiac murmurs in infancy the authors record their observations on 630 ostensibly healthy children examined at the ages of about 6 weeks, 3, 6, 9, and 12 months, and thereafter at 6-monthly intervals, most of them for about 3 years. Regular 6-monthly radiographic examinations were made in all children. Thirty-two (5 per cent) had murmurs which were classified according to the age when first noticed and are described as transient, temporary, or persistent. No diastolic murmurs were observed. Of the 32 murmurs 23 were not detected until after the child was 9 months old. There was a relatively greater number of transient murmurs among infants observed in the early weeks of life. Six out of 8 murmurs appearing at the age of 18 months remained permanent. With the exception of 2 cases, no associated symptoms or signs could be observed. No correlation between clinical findings and radiographic appearances could be established. The results are as yet too few to allow any conclusions to be drawn. *H. Herlinger*

1587. **The Function of Vernix Caseosa in the First Days of Life of the Newborn Infant.** (Funkcia plodového manu v prvych dzoch života novorodenca.)

By E. Dlhos. *Ceskoslov. Gynaek.*, **12**, 399–410, 1947. 3 figs., 7 refs.

Stimulated by observation of an epidemic of pemphigus neonatorum which was brought under control after the daily bath had been discontinued, the author compared the findings in 300 babies whose vernix caseosa was left and rubbed into the skin, and in an equal number of babies given as usual daily baths. The effect on the initial loss of weight, body temperature, icterus, and skin affections was noted. The lowest body weight was reached 3.76 days after birth in the experimental group and 4.05 days after birth in the control group. A higher percentage of controls (4 per cent) lost over 15 per cent of their birth weight; in the experimental group 1.3 per cent lost this amount. Temperatures from 37° to 38°C. (98.6° to 104.4°F.) were recorded in 65 per cent of the controls against 27.66 per cent of the babies whose vernix was not removed. The incidence of icterus was higher in the experimental group (33 per cent against 22.33 per cent); but skin affections were found in only 1.66 per cent of the unbathed babies against 9.63 per cent of the controls. This last finding is explained by the fact that the vernix caseosa protects the skin against drying, fattens it, changes its pH towards acidity, and supplies biologically important material, mainly sulphur. *In vitro* experiments did not, however, show any bactericidal or bacteriostatic activity of the vernix. From these observations and from data found in the literature the author recommends preservation of the vernix caseosa, especially in premature babies.

A. Rohan

1588. **Premature Closure of the Cranial Sutures.**

By D. R. Simmons and W. T. Peyton. *J. Pediat.*, **31**, 528–547, Nov. 1947. 5 figs., 54 refs.

Various surgical procedures, mostly unsuccessful in altering the patient's ultimate disability and often attended by a considerable mortality rate, have been described for the treatment of craniostenosis in its various forms. Many disappointments have been due to failure to recognize the fact that the patients suffered from microcephaly with mental retardation but without signs of raised intracranial pressure, and were not cases of true craniostenosis. The growth of the cranium is dependent on, and normally keeps pace with, the growth of the brain, which has practically reached its adult size by the age of 3 years. Early closure of sutures after this age will result in alteration in shape of the skull but will have little effect on mental development, whereas if it occurs earlier and the brain is growing normally papilloedema, visual impairment, mental retardation, epilepsy, headache, and other signs of increased intracranial pressure develop. In typical oxycephaly (pointed skull), exophthalmos and divergent squint due to shallow orbits and divergence of the visual axes occur also. Commonly associated congenital abnormalities, such as syndactyly and mongolism, argue in favour of the theory that an inherent defect in the germ plasm is a cause of this condition. There is also a distinct tendency for it to be familial and inherited.

The authors stress the fact that clear signs of increased intracranial pressure occur late in the condition, and that optic atrophy is also a late sign

and secondary in most cases to papilloedema. The optimum time for successful surgical treatment is before cerebral damage occurs. Retardation of mental development may be recognized in the early months of life and the authors consider this to be the indication for surgical intervention in a patient with a skull deformity and radiological evidence of synastosis. [It is difficult, however, to see how the cases of the microcephaly with early closure of sutures can be differentiated.]

Subtemporal decompression and various other operations have been designed for the relief of craniostenosis. Linear craniectomy—that is, removal of strips of bone along the prematurely synastosed sutures—has given promising results, especially in young infants, whose skull bones are thin and flexible. On the other hand bridges of bone tend to occur across the artificial sutures, and expansion of the skull is thus arrested. The authors describe a method of interposing tantalum foil between the bone edges to prevent this regeneration. In older children with thick skulls the multiple groove method known as morcellation is preferable, and in adults with visual disturbances and headache subtemporal decompression is recommended. Decompression of the optic canal is not generally indicated but may be considered in certain cases in which direct pressure on the optic nerves may be suspected or in which decompression has failed to arrest progressive loss of vision.

M. Baber

1589. **Duration of Pregnancy and Birth Weight.** (Schwangerschaftsdauer und Neugeborenengewicht.)

By H. A. HOSEMANN. *Arch. Gynäk.*, **176**, 109–123, 1948. 6 figs., 20 refs.

1590. **Duration of Pregnancy and Size of Foetus at Birth.** (Schwangerschaftsdauer und Neugeborenengrösse.)

By H. A. HOSEMANN. *Arch. Gynäk.*, **176**, 124–134, 1948. 4 figs.

1591. **The Etiological Factors of Asphyxia Neonatorum.**

By R. L. MEANS. *J. Bowman Gray Sch. Med.*, 6, 48–53, Apr. 1948. 31 refs.

1592. **The Pathogenesis of Congenital Polycystic Lung and its Correlation with Polycystic Disease of other Epithelial Organs. Reconstruction of Cystic Elements in Two Cases.**

By R. F. NORRIS and R. M. TYSON. *Amer. J. Path.*, **23**, 1075–1097, Nov. 1947. 9 figs., 35 refs.

Two cases of congenital cystic disease in newborn infants are described. In the first the right lung was enlarged by cysts. These did not communicate with the bronchus, the immediate branches of which ended abruptly. The cysts and the connected alveoli were filled with fluid. The lung also contained isolated bronchial tubes which were not dilated and which were connected with atelectatic alveoli. In the second case there was a large cyst in the left upper lobe. The left upper lobe bronchus ended blindly and the cyst had no alveolar connexions. In the left lower lobe the small bronchi showed irregular sacculations with abnormal alveolar communications. The authors have written a series of articles on cystic disease in other organs and they discuss its pathogenesis. The degenerative process which leads to isolation and cyst formation in the more distal parts of the developing bronchial tree they designate "segmentation". They are uncertain whether in cystic disease of the lung there is an excess of bronchi and whether the cysts represent a persistence of embryonic bronchi which normally are resorbed. They also raise the question of deficiencies of the circulation in the origin of the condition. [A thesis entertained by the abstracter.] A vascular anomaly was possibly responsible for the large cyst in the second case, in which the heart and large vessels were transposed. *D. M. Pryce*

1593. **Medullary Malformation in a 25-mm. Embryo, and its Importance in the Pathogenesis of Hereditary Ataxia.** (Malformación medular de un embrión de 25 milimetros, y su importancia en la etiopatogenia de la heredo-ataxia.)

By F. ORTS LLORCA and M. M. MARTINEZ. *Rev. clin. esp.*, **28**, 40–44, Jan. 15, 1948. 7 figs., 15 refs.

The embryo examined and studied by the authors showed a severe malformation, mainly abnormal shape of the cord, the dorsal part of which was adherent to the perimedullary tissues. This had prevented the normal development of the tracts of Goll and Burdach. The perimedullary space was completely absent; the meninges, too, were malformed. The authors believe that similar lesions would produce later on clinical pictures of status dystrophicus and Friedreich's hereditary ataxia. *F. K. Kessel*

1594. **Congenital Malformations Induced in Rats by Maternal Vitamin A Deficiency. II. Effect of Varying the Preparatory Diet upon the Yield of Abnormal Young.**

By J. WARKANY and C. B. ROTH. *J. Nutrit.*, **35**, 1–11, Jan. 1948. 4 figs., 9 refs.

Warkany and Schraffenberger reported congenital anomalies of the eyes in the offspring of rats depleted of vitamin A. Since the rate of fertility was low in the original experiments and the yield of abnormal offspring small, modifications of the preparatory diet were studied.

Female rats were placed on the preparatory diet (diet U): ground whole wheat, 74 per cent; crude casein, 15 per cent; brewers' yeast, 10 per cent; sodium chloride, 1 per cent. According to the supplements added to this diet the animals were divided into four groups: Group I: diet U with 2 g. of frozen horsemeat daily and 4μg. of carotene every tenth day was given to 165 females until mating occurred, then replaced by diet W. Group II (34

females): diet U daily with 12 μg. of carotene every tenth day; Group III (33 females): diet U daily with 25 μg. of carotene every tenth day; Group IV (28 females): diet U daily with 25 μg. of carotene every tenth day during the first month; in the following month a loss of weight was observed and therefore the carotene intake was doubled during the last 2 weeks of the fertility period. Groups II, III, and IV were placed on diet W. upon reaching maturity and attempts were made to breed from them after the change. Diet W was a purified diet completely free from vitamin A and carotene, with small measured amounts of the other vitamins added.

When early termination of pregnancy threatened the foetuses were removed. When the young were carried to term foetuses were removed on the twenty-second day of gestation. Many young thus removed were alive but none could be reared. The eyes of at least 1 animal in each litter were sectioned serially. If no retrolenticular membrane was found the animal was considered normal, but if a membrane was seen in any section the animal was regarded as abnormal. When the eyes of one foetus in a litter were found to be abnormal the entire litter was considered and counted as abnormal. This method of classification appeared to be justified.

Of 260 females 22 had cycles but did not mate; 124 mated but had no issue; 114 had litters but only 30 of these litters were carried to term; 89 litters were considered abnormal and 25 normal. These litters consisted of a total of 820 young, 612 of which were regarded as abnormal and 208 as normal. Other ocular defects were seen in many of the eyes sectioned. A number of litters showed external changes not observed in control animals —smallness of size, " convex " back, " open eyes ", puffiness of hands and feet. In many foetuses with abnormal eyes serial section of the trunk and abdomen revealed various congenital anomalies of the soft tissues. Abnormalities of the same type were seen in all four groups. In Groups I and II there were the lowest fertility rate and the highest incidence of abnormal young; Group IV had the highest fertility rate and the lowest incidence of abnormal young. In 80 females used as controls, no abnormalities were seen in litters.

It is concluded that variations in the preparatory diets influenced the proportion of abnormal young.

Joseph Parness

1595. **Congenital Ocular Anomalies Resulting from (a) Premature Birth (b) Rubella Infection of Mother During Pregnancy.**

By W. R. BUFFINGTON. *New Orleans med. Surg. J.*, **100**, 466–470, Apr. 1948.

1596. **Radiological Features of Anencephaly.** (Aspecto radiológico das anencefalias.)

By H. COSTA. *An. brasil. Ginec.*, **13**, 189–194, Mar. 1948. 3 figs., 11 refs.

1597. **Further Observations on Congenital Malaria.** (Weitere Beobachtungen zur Frage der angeborenen Malaria.)

By A. ECKSTEIN. *Ann. paediatr., Basel*, **169**, 381–403, Dec. 1947. 2 figs., 8 refs.

The author reports 4 cases of congenital malaria, which raise the number of similar cases observed by him to 18. The difficulties in diagnosis of congenital malaria are mainly due to the peculiarities of the course of malaria in the neonatal period and in early infancy. Many workers consider that the diagnosis of congenital malaria is justified only when the parasites are found in the blood of the umbilical cord of the infant during the first days of life. This concept, based on the assumption of a fixed incubation period, is not accepted by the author, since a long incubation period may delay for months or even years the appearance of definite signs and symptoms. For this reason the following three points are considered important in the diagnosis: (1) The mother must be suffering from malaria. Of particular importance are attacks during the last few months of pregnancy or immediately before or during labour. The plasmodia of mother and child must be of the same variety. (2) Presence of plasmodia in the blood of the infant during the neonatal period or during infancy, together with symptoms of malaria, with special regard to the clinical forms which are characteristic of infancy and which have been previously described by the author. (3) The infant must be living under conditions which exclude the possibility of a postnatal infection. This exclusion is usually possible during periods when the average temperature is below 15°C. and development of the parasites in the mosquito consequently stops. This last condition prevails during many months of the year in Ankara, where the author has been collecting his observations. He has thus been able to diagnose congenital malaria in at least 10 out of 25 infants with malaria in a residential nursery. He concludes by stressing the importance during pregnancy of intensive prophylaxis against malaria in endemic areas. The possibility of antenatal infection of the infant when the mother has a history of malaria should always be borne in mind, and doctors in endemic areas should become familiar with the peculiarities of malaria in infancy.

S. Doxiadis

1598. **Persistent Pleuro-peritoneal Cavity (False Diaphragmatic Hernia) in the Newborn.** (Cavum pleuroperitoneale persistens (Hernia diaphragmatica spuria) bei neugeborenen.)

By P. O. PARNANEN and H. HAAPOJA. *Acta obstet. gynec. scand.*, **27**, 407–417, 1948. 2 figs., 49 refs.

1599. **Diabetes Mellitus in Infants under One Year of Age. Report of a Case and Review of the Literature.**

By J. SCHWARTZMAN, M. E. CRUSIUS, and D. P. BEIRNE. *Amer. J. Dis. Child.*, **74**, 587–606, Nov. 1947. Bibliography.

In a girl, aged 8 months, admitted to hospital for acute bronchitis, routine tests of urine revealed sugar and acetone. Diabetes mellitus, suggested by a history of this disease in a maternal aunt and cousin, was confirmed by the finding of a blood-sugar level of 600 mg. per 100 ml. and by subsequent glucose tolerance tests. One injection of 20 units of insulin was followed by a clinical hypoglycaemic reaction, but thereafter during the 7-month period of observation no insulin was necessary. Septic complications—abscess formation and, later, pharyngitis and gingivitis—were overcome by systemic administration of penicillin. Dextrose tolerance curves in both parents and in 6 other children were normal.

[The series revealed a worse prognosis than can reasonably be expected in these days of early diagnosis and correct treatment. The author's plea for routine dextrose tolerance tests on any infant with a family history of diabetes "every two months for the first year and every six months thereafter" seems unwise, since most parents of such children make the diagnosis for themselves and are only too apprehensive of early symptoms.]

H. Whittaker

1600. **Penicillin in the Treatment of Gonococcal Ophthalmia of the Newborn and of Septic Endophthalmitis.** (La penicilina en el tratamiento de la oftalmia gonocócica del recien nacido y en la endoftalmitis séptica.)

By E. DALGADO BENAVIDES. *Arch. Soc. oftal. hisp.-amer.*, **7**, 1121–1128, Nov. 1947.

The author states that although penicillin modifies the picture in panophthlamitis, it has no advantages over the sulphonamides. Even when systemic administration is combined with subconjunctival, anterior-chamber, and intra-vitreous injections, the results are no better. He has found that the most severe cases of gonococcal ophthalmia improve with repeated irrigations of boiled water and injection of penicillin (5,000 units). After the third injection of penicillin the oedema disappears, and the gonococcus is no longer found in the pus.

E. E. Cass

1601. **Oral Penicillin in Young Children.**

By A. I. SUCHETT-KAYE and R. B. LATTER. *Brit. med. J.*, **2**, 953–954, Dec. 13, 1947. 4 refs.

Calcium penicillin tablets were given in doses of 10,000 to 20,000 units every 3 or 4 hours for infants under 6 months, 20,000 to 30,000 units for children of 6 to 12 months, and 30,000 to 40,000 units for those over 1 year. Eighteen cases of bronchopneumonia and 5 cases of lobar pneumonia were treated, but in 4 treatment was interrupted by complications and in 4 others treatment with sulphamezathine was instituted in view of failure to respond to oral penicillin. The remaining patients made a satisfactory recovery. Adequate penicillin levels were usually present in the serum 2 hours after an oral dose. [There is little evidence in this paper of the extent of the influence of oral penicillin on the course of the disease.]

J. W. Litchfield

1602. **Treatment of Infantile Diarrhoea by Streptomycin.** [In English.]

By P. LEISTI. *Ann. Med. intern. fenn.*, **36**, 575–583, 1947. 1 ref.

The mortality rate in cases of infantile diarrhoea treated in the Children's Clinic, Helsinki University, has in recent years varied from 20 to 59 per cent. Penicillin having proved ineffective, streptomycin has been tried since June 1947, though only in the most severe cases. The drug has been given in doses of 5,000 to 20,000 units intramuscularly at 3-hourly intervals. Conventional treatment for dehydration was carried out concurrently. In 38 full-time infants, aged from 1 to 9 months, there were 8 deaths. In 11 cases in which streptomycin was given only after other treatment had been applied without result, the effectiveness of the drug was apparent. As judged by time of recovery, recovery of weight, and number of days in hospital, streptomycin proved beneficial in the majority of cases treated, although in 5 fatal cases it seemed without effect. All of 8 premature infants recovered; in 2 of these streptomycin was given orally and appeared as effective as by the intramuscular route.

D. Gairdner

1603. **Epidemic of Salmonellosis Among Infants due to *Salmonella enteritidis*.** (Epidemia duru rzekomego wśród niemowlat wywolana paleczka Gaertnera.)

By A. KANSKI, I. MOSZKOWSKA, and Z. SKURSKA. *Polsk. Tyg. lek.*, **2**, 1354–1359, Nov. 24, 1947. 5 refs.

The authors give a detailed report of an epidemic caused by *Salmonella enteritidis* (Gärtner), observed among infants during the winter of 1947 in Breslau. The 40 cases which occurred could be divided into: (1) cases of gastro-entero-colitis; (2) cases of septicaemia. In the first group the organism was isolated from the stools from the ninth to the seventieth day of the illness. The agglutination tests were positive on the twenty-first day in most cases, but in one case the test was positive as early as the fourth day. The gastro-entero-colitis lasted about 4 months and gradual recovery followed. More severe symptoms were met with in the septicaemic group. In infants between 6 weeks and 6 months severe symptoms of general toxaemia occurred without any gastro-intestinal signs. Meningitis and cerebral abscesses were often encountered. In the majority of cases the organism was identified in the cerebrospinal fluid. In isolating the bacillus bone-marrow cultures were found to be more reliable than those from blood.

In this group of cases no treatment was of any avail and all the infants died. Both sulphonamides and penicillin were found to be useless.

J. T. Leyberg

1604. **Neonatal** *Bact. Coli* **Meningitis after Prolonged Labour.**

By H. R. Duval and J. T. Burrowes. *Brit. med J.*, **1**, 1180–1182, June 19, 1948. 25 refs.

1605. **Vitamin C in the Blood and Urine of the Newborn and in the Cord and Maternal Blood.**

By B. M. Hamil, B. Munks, E. Z. Moyer, M. Kaucher, and H. H. Williams. *Amer. J. Dis. Child.*, **74**, 417–433, Oct. 1947. Bibliography.

The plasma concentration of reduced ascorbic acid was estimated in samples of cord blood, capillary blood from 24 male breast-fed infants, and venous blood from their mothers, and compared with the amounts of vitamin C excreted in the infant's urine during the first week of life. The results obtained showed wide variations, but cord blood contained by far the highest concentration of vitamin C, and the average value for the babies' blood, though only about half that for cord blood, was higher than that for mothers' blood. Concentrations of vitamin C in urine were high during the first 2 days of life, but if the babies were not supplied with vitamin C urinary excretion dropped rapidly to low levels or disappeared as the blood level of the vitamin decreased. Vitamin C is thought to exercise a function in cell chemistry, and if this is so presumably more of the vitamin would be required during the state of low oxygen tension of the blood in intrauterine life than after birth, at which time changes in renal function contribute to abundant urinary excretion.

M. Baber

1606. **Acute Anaemia of the Newborn Due to Subaponeurotic Cephalhaematoma.** (Anemia acuda del recién nacido por cefalohematoma subaponeurótico.)

By G. Gil. *Rev. chil. Pediat.*, **18**, 855–862, Nov. 1947. 1 fig., 7 refs.

1607. **Inclusion Bodies (Protozoon-like Cells) in the Organs of Infants.**

By D. F. Cappell and M. N. McFarlane. *J. Path. Bact.*, **59**, 385–398, July, 1947. 10 figs., bibliography.

The previous literature is reviewed and analyzed. Two cases are recorded here. Both infants had clinical signs of haemolytic disease of the newborn but in neither was it possible to show that there had been *iso*-immunization of the mother. Significantly, the mother of the first infant had a subsequent normal child (her fourth), while in the second case the infant was a first child. Both infants showed obvious extramedullary haematopoiesis and the presence of inclusion bodies in various epithelia, such as renal tubules, bile ducts, pancreas, or pulmonary alveoli. [The morphology of the bodies is fully described and the illustrations are excellent.] The bodies resemble closely the salivary-gland inclusions seen in various animals, including man, and the suggestion is made that these cases may be examples of the generalization of salivary virus which can be produced experimentally in animals.

Such infants were generally considered to have congenital syphilis; since then the clinical picture seen in most of these cases has been called haemolytic disease of the newborn. It therefore seems likely that many, although not all, of the infants showing inclusion bodies had the clinical picture which to-day we know to be characteristic of Rhesus incompatibility. It is now demonstrated that in the disease under discussion no such Rhesus incompatibility can be demonstrated. The important question is raised whether the inclusion bodies and the haemolysis may both be due to a virus infection. The close-knit argument on histological and serological grounds seems to lead to the inescapable conclusion that another disease has been discovered.

[This is the first report in the British literature on the subject and is a paper that should be read.]

A. C. Lendrum

1608. **Erythroblastosis Foetalis without Rhesus-incompatibility.** (Erythroblastosis foetal zonder rhesus-antagonisme.)

By H. Hoyng. *Ned. Tijdschr. Geneesk.*, **91**, 3653–3655, Dec. 13, 1947.

The following case is described to show that Rh-incompatibility is by no means the only cause of erythroblastosis foetalis. A woman, aged 39, with a contracted pelvis, gave birth in the thirty-sixth week of her tenth pregnancy, after induction of labour, to a child suffering from foetal hydrops; the child died soon afterwards from erythroblastosis foetalis. Both mother and father were Rh-positive and both belonged to the blood group O. Clinical and laboratory investigation eliminated the possibility of syphilis, diabetes, and renal disease. The infants of the first five pregnancies were born alive and remained well; the first 2 were born at term with forceps application and for the other 3 premature labour was induced; 1 of them had jaundice after birth. The sixth child, also delivered after induction of labour, had jaundice and died 3 days after birth. The seventh, eight, and ninth children were stillborn between the seventh and eighth months of pregnancy; they were, according to the mother, " thick and swollen ".

A. Lilker

1609. **Iso-immunization as a Cause of Erythroblastosis (4 Cases Due to the Rh Factor).** (Iso-immunisation als Ursache der fetalen Erythroblasten-krankheiten (Mit 4 durch den Rh-faktor bedingten Fällen).)

By P. Pfau. *Klin. Wschr.*, **26**, 132–136, Mar. 1, 1948. 1 fig., 30 refs.

1610. **The *iso*Leucine Requirement of the Infant.**

By A. A. ALBANESE, L. E. HOLT, V. I. DAVIS, S. E. SNYDERMAN, M. LEIN, and E. M. SMETAK. *J. Nutrit.*, **35**, 177–183, Feb. 10, 1948. 1 fig., 6 refs.

In order to determine whether the higher requirement of infants for nitrogen is due to the limiting factor of a single amino-acid or to a higher demand for all of the amino-acids, it is necessary to carry out "balance" experiments with single amino-acids. In this paper experiments with *iso*leucine are recorded. Five normal healthy male infants of 4 to 10 months were fed on a hydrolyzed beef haemoglobin as a source of protein. On a diet low in *iso*leucine there was a big decrease in nitrogen retention. In 3 infants this was made good by 120 mg. per kilo per day. Two other infants were tested with levels of 60 and 90 mg. of *iso*leucine per kilo per day; the former showed a low retention of nitrogen while in the latter retention was normal. It is deduced that the requirements of *iso*leucine are approximately 90 mg. per kilo per day. Unlike deficiency of tryptophan, deficiency of *iso*leucine had no effect on the level of plasma protein or of haemoglobin. This is of interest in that both of these proteins are low in *iso*leucine. *J. Yudkin*

1611. **Thiamine, Riboflavin, Nicotinic Acid, Pantothenic Acid and Biotin in the Urine of Newborn Infants.**

By B. M. HAMIL, M. CORYELL, C. RODERUCK, M. KAUCHER, E. Z. MOYER, M. E. HARRIS, and H. H. WILLIAMS. *Amer. J. Dis. Child.*, **74**, 434–446, Oct. 1947. 2 figs., 41 refs.

Estimations of the daily urinary excretion of the vitamins of the B complex were undertaken in newborn infants as a preliminary to assessing the nutritional status of the babies as regards these substances. A wide range of concentrations was found in specimens collected from different infants and even from the same infant during the first few days, but maximal average concentrations of thiamin and of pantothenic acid were found in urine excreted on the third day of life. For riboflavin the maximal average value was found on the first day, and for nicotinic acid and biotin on the second day. The concentration of all vitamins in the urine decreased greatly after the first few days, very low levels being reached by the fifth day postpartum in spite of abundant intake of breast milk. This large excretion of vitamins presumably indicates a high foetal storage, which may be related to the intrauterine state of low oxygen tension. Changes in pH or oxygen tension, or other physical factors which occur at birth, may be responsible for the excretion of vitamins in the neonatal period; as the latter may be related to purely physiological changes in renal function at birth. *M. Baber*

1612. **Some Observations on the Artificial Feeding of the Normal Infant.**

By W. EMDIN. *S. Afr. med. J.*, **22**, 313–315, May 8, 1948.

1613. **Concentrated Human Milk.** (Latte umano concentrato.)

By A. BIEBER. *Riv. Clin. pediat.*, **45**, 577–604, Oct. 1947. 23 figs., 13 refs.

Human milk was concentrated by boiling at 55°C. under reduced pressure until the volume was halved. It was then stored in a refrigerator. There was no alteration in taste or smell. Average values were: for protein 2.1 per cent, fat 5.8 per cent, sugar 13 per cent, vitamin C 80 to 160 mg. per litre. Microscopically, there was a great preponderence of small fat globules. The concentrate was used for infants in addition to the routine milk feeds. Quantities varying from 30 g. to 100 g. daily, according to the size of the main feed, were given to 22 infants—18 premature and 4 weakly babies. In all there was an immediate upward movement in the weight curve. Compared with other babies in the clinic given the same care and routine feeding, there was a pronounced increase in the rate of development. The weight was doubled in 60 to 70 days, instead of 90. The author believes that the good result was partly due to the fact that the diet became adequate as regards essential proteins. The daily amount required, according to Levine, is 4.4 to 6 g. for a baby weighing less than 2 kg. This amount is not secured with the usual feeds given to premature infants, but is attained on adding concentrated milk. The improvement in the appearance of these babies was striking, apart from the actual gain in weight.

[It is difficult to share the author's belief that the infant benefits from the increase in protein, since the value is raised only very slightly by this feeding method. It is also not clear whether there was any selection of cases. If there was not, there must have been some other reason for the failure of so many premature infants to thrive.]

J. G. Jamieson

1614. **Investigations on the Preservability and Preservation of Mother's Milk. Preliminary Report.** [In English.]

By E. SELESTE. *Ann. Med. intern. fenn.*, **36**, 630–646, 1947.

The influence of various factors upon the preservability of human and cows' milk was studied by measuring decreases in the pH of milk samples over periods of 5 days, since bacterial growth tends to acidify milk. The following were the main conclusions reached; in general, these applied whether the milk was preserved at −5.5°C., at 20°C., or at 37°C. Human milk drawn from breasts cleansed with spirit keeps better than milk from breasts which are merely washed with water. Heating human milk to 80°C. for 2 minutes impairs its preservability; the reverse is true of cows' milk. On the other hand, when human or cows' milk is heated to 62°C. for 20 minutes preservability is improved. When a culture of lactic-acid-producing organisms is added to human milk which has

previously been heated to 62°C. for 20 minutes, the milk keeps better than milk which has not been previously heated. These results can be accounted for by assuming the presence of a "lysozyme" in both human and cow's milk, activation of which by moderate heat causes the destruction of bacteria.

D. Gairdner

1615. **Mortality Increase in Post-mature Infants.** (Die Übersterblichkeit der Kinder bei übertragenen Schwangerschaften.)

By W. BICKENBACH. *Geburtsh u. Frauenheilk.*, 7, 3–7, Oct. 1947. 1 fig., 7 refs.

The author reviews some recent literature on the subject of foetal mortality in association with prolonged pregnancy. He presents in a graph the results in such cases at the Münster Clinic from 1924 to 1942, 4,000 pregnancies of more than 279 days' duration from the first day of the last menstrual period being analyzed. The curve of foetal mortality rises sharply from 298 days onwards (1.09 per cent at 282 days to 2.83 per cent at 294 days and 25 per cent at 315 days). A plea is made for medical induction of labour at 285 days; if pregnancy goes on to 295 days this should be followed by surgical induction.

Kenneth Bowes

1616. **Excess of Male Births and Excess of Male Infant Mortality.** (Knabenüberschuss und Knabenübersterblichkeit.)

By H. HOSEMANN. *Geburtsh. u. Frauenheilk.*, 7, 65–77, Nov. 1947.

The paradox that the "weaker sex" is the stronger has long been observed by the obstetrician. The author, using statistical material from the University Women's Clinic at Göttingen, has considered the implications of this in pregnancy and childbirth. Out of about 20,000 deliveries (1926 to 1945) 11,000 were found to be completely normal as regards pregnancy and childbirth, and this "physiological" series has been analyzed in some detail. The series yielded a sex proportion of 107.5 males to 100 females at birth (cf. European total of 106 : 100). About 40 per cent of the births occurred during the war years and the sex proportion was 104 to 113 males to 100 females. Before the war the ratio was less. The older the mother the greater the chance of her having a female child; when the mother was under 19 the ratio was 115 : 100, when she was 19 to 29 it was 108 : 100, when she was 29 to 39 it was 92 : 100, and over the age of 40 it was 44 : 100. Increasing parity, particularly between the third and fifth pregnancies, increases the proportion of male babies (para-1, 106 males; para-3, 112 males; para-4, 122 males).

The stillbirth rate, neonatal mortality rate, and mortality rate in immature births were higher for male children. In the total series the sex ratio for mortality was 179 males : 100 females; this may be associated with the increased cephalic measurements of the male and his greater birth weight. Caesarean section was found to be significantly more common if the foetus was male, as also was forceps delivery. The sex ratio in the latter was 152 : 100. The male foetus is more liable to asphyxia and less able to withstand it. The total forceps mortality rate was 6.3 per cent in 1,206 cases (6.8 per cent in males, 5.8 per cent in females). A further associated factor influencing the sex ratio was found to be the type of menstrual cycle in the mother. With a "normal" 28-day cycle the sex ratio was 106 : 100; with a lengthened cycle it was 146 : 100.

Kenneth Bowes

1617. **Illness Among Infants, with Comparative Mortality Data.**

By S. D. COLLINS. *Publ. Hlth. Rep., Wash.*, 63, 637–662, May 14, 1948. 13 figs., 16 refs.

1618. **Bronchial Obstruction in the Newborn. Intrauterine Suffocation.** (L'obstruction bronchique du nouveau-né. La suffocation intra-utérine.)

By L. DEROBERT. *Presse méd.*, 56, 444–445, June 23, 1948. 6 figs., 1 ref.

1619. **Obstetric Operative Trauma as a Factor in Foetal and Neonatal Mortality.** (Do tráuma operatório obstétrico como fator de mortalidade natal e neonatal.)

By E. BRAGA. *Rev. Ginec. Obstet.*, 1, 241–246, Apr. 1948. 16 refs.

OBSTETRIC OPERATIONS

1620. **Some Considerations on Caesarean Section.** (Algunas consideraciones sobre operación cesárea.)

By H. C. SOTO. *Bol. Soc. chil. Obstet. Ginec.*, 12, 283–295, Nov. 1947. 28 refs.

1621. **A Study of Ten Years of Cesarean Sections at Emanuel Hospital.**

By C. L. FEARL. *West. J. Surg. Obstet. Gynec.*, 56, 290–297, May 1948. 16 refs.

1622. **282 Cases of Caesarean Section.** (Commentario sobre 282 casos de cesarea.)

By P. JOFRE. *Bol. trim. Hosp. Vina d. Mar.*, 4, 45–51, Apr. 1948. 11 refs.

1623. **The Outlook for the Infant after Caesarean Section.** (L'avenir des enfants nés par césarienne.)

By P. LANTUEJOUL and P. JANNY. *Bull. Acad. nat. Méd., Paris*, 132, 146–148, Mar. 2, 1948. 2 figs.

1624. **Shortened Cord as an Indication for Caesarean Section and Other Obstetric Operations.** (Uber die durch zu kurze oder verkürzte Nabelschnur bedingte Indikation zum Kaiserschnitt und zu anderen geburtshilflichen Operationen.)

By F. v. KUHBACKER. *Geburtsh. u. Frauenheilk.*, 8, 372–376, Apr. 1948.

1625. **The Pfannenstiel Incision for Cesarean Section.** By D. W. DECARLE and R. B. DURFEE. *West. J. Surg. Obstet. Gynec.*, **56**, 360–364, June 1948. 4 refs.

1626. **Symphysiotomy in the Antibiotic Age.** (La sinfisiotomia en la era antibiótica.) By A. P. RAMOS. *Obstet. Ginec. lat.-amer.*, **6**, 3–12, Jan.–Feb., 1948. 4 refs.

GYNAECOLOGY

General.

1627. **The Blood Glutathione and Oxidative-reduction Processes in Gynaecological Conditions.** [In Russian.] By F. D. ANISKOVA. *Akush. Ginek.*, No. 2, 10–15, 1948.

1628. **Analysis of the Causes of Death in Gynaecological Conditions.** [In Russian.] By M. A. DANIAKHI and Z. I. GUREVITCH. *Akush. Ginek.*, No. 2, 35–42, 1948.

1629. **Iron Deficiency in Gynaecology.** (Les aspects de la carence en fer dans la pratique gynécologique.) By J. A. SCHOCKAERT, J. P. HOET, M. RENAER, and J. LEDERER. *Brux.-méd.*, **28**, 1150–1156, June 6, 1948.

Disorders of function

1630. **Artificial Reproduction of the Cyclic Changes in Cervical Mucus in Human Castrates, with Clinical Correlations.** By A. R. ABARBANEL. *West. J. Surg. Obstet. Gynec.*, **56**, 26–34, Jan. 1948. 2 figs.

The results of this investigation are listed under four headings. In the first of these, the cyclic changes in cervical mucus during the normal menstrual cycle were observed. In the post-menstrual phase (days 5 to 9 of the cycle) the mucus was noted to be opalescent, to contain polymorphonuclear leucocytes, and to be of a somewhat gelatinous consistency. Spermatozoa did not usually penetrate this mucus, but if they did they were very quickly bogged down so that at the end of an hour or so they were immobile and had only traversed a few millimetres. In the pre-ovulatory phase (days 10 to 15 of the cycle) well-marked changes took place in the character of the mucus at or about the time of the ovulatory dip in basal body temperature. There was increase in volume and decrease in viscosity, and leucocytes disappeared almost completely. If leucocytes persisted then endocervicitis was almost invariably present. At this time spermatozoa penetrated easily and rapidly in great numbers. In cervical mucus at this stage spermatozoa usually lived for 24 to 72 hours. When the post-ovulatory phase was studied (days 16 to 28 or 30) the cervical mucus had decreased in amount and increased in viscosity, and repelled the penetration of spermatozoa, which rapidly became immobile and then immotile. Menstrual fluid was easily and rapidly penetrated by spermatozoa which remained actively motile for 24 to 48 hours in it.

In the second group the effects of various oestrogens and progesterone were investigated. These substances were given to suitable hysterectomized, bilaterally ovariectomized women who had an apparently normal cervical stump. The changes of the proliferative phase could be reproduced exactly when oestrogen preparations were given, and the post-ovulatory or luteal phase when progesterone was administered but only provided that it had been preceded by an oestrogen. Progesterone itself had no effect on the cervical mucus. In the presence of endocervicitis (group 3) the cervical mucus was found to be viscid and generally scanty. Leucocytes were present and clumped in large aggregates but, strangely enough, slight variations in volume and viscosity were noted at or about mid-cycle. The author believes that endocervicitis results in the loss of fluid (? water) by the mucus with resultant increase in viscosity. In the fourth group, experiments were made on the penetration by spermatozoa of mucus which had been sealed in a capillary tube and mucus which had been exposed to the air at room temperature. Almost invariably the mucus from the sealed tube was easily penetrated by spermatozoa, even after such a lengthy period as 2 weeks. With the exposed mucus penetration did not take place.

The author concludes with some practical clinical points dealing with the post-coital test (Smith-Sims-Huhner test), endocervicitis, pin-point os, and scanty or absent mucus in mid-cycle. The post-coital test should be performed on the eleventh, fourteenth, and (if necessary) seventeenth day of the cycle. Treatment of endocervicitis by conization of the cervix is advised and, if necessary, artificial insemination with the husband's semen beyond the endocervix. Pin-point os is rarely responsible for infertility, and scantiness or absence of mucus in mid-cycle may follow extensive cauterization of the cervix or may be congenital. It is noted that when tubal insufflation is performed with the olive of the cannula pressed home into the cervical canal, dilatation of the canal takes place with consequent pouring forth of cervical secretions. In the author's opinion, therapeutic success should be ascribed to this effect rather than to the bubbles of carbon dioxide gurgling through the tubal lumen.

E. L. Nicolson

1631. **Preparations of Female Sex Hormones and Their Use in Gynaecology.** [In Russian.] By K. P. PREOBRAZHENSKI. *Akush. Ginek.*, No. 2, 27–35, 1948.

1632. **Studies on Antihormone Specificity with Particular Reference to Gonadotropic Therapy in the Female.**

By J. H. LEATHEM and A. E. RAKOFF. *J. Clin. Endocrinol.*, **8**, 262–268, Mar. 1948. 8 refs.

1633. **Ethinyl Estradiol.**

By C. H. BIRNBERG, S. H. LIVINGSTON, L. KURZROK, and D. A. SHERBER. *Amer. J. Obstet. Gynec.*, **54**, 855–860, Nov. 1947.

The effect of ethinyl oestradiol was observed (1) in the menopause; (2) in amenorrhoea, primary and secondary; (3) in suppression of postpartum lactation; and (4) in labour. In menopausal cases up to three 0.05-mg. tablets of ethinyl oestradiol were administered daily, depending upon the severity of the symptoms; 45 patients (79 per cent) had complete relief from menopausal symptoms, 10 patients (17 per cent) had moderate relief, and 2 patients (4 per cent) had no relief. For amenorrhoea, 0.05 mg. ethinyl oestradiol was given daily for 20 days, followed by a 10-day interval. The duration of treatment was from 4 to 6 months; patients bled periodically, and there was growth of the uterus and cervix. Eight patients bled regularly after treatment was stopped; in 6 of these, aged between 18 and 21 years, biopsy revealed secretory endometrium. For inhibition of postpartum lactation in non-nursing mothers 30 tablets of ethinyl oestradiol, 0.05 mg., were given over a period of 9 days. In 85 (58 per cent) there was suppression of lactation; results were good in 23 patients (16 per cent), fair in 22 (16 per cent), and poor in 15 (10 per cent). The same dose was used in 26 [*sic*] nursing mothers with complete suppression in 6 patients, partial suppression in 17, and no suppression in 6. A dose of 6 tablets of ethinyl oestradiol, 0.05 mg., was given every 2 hours for up to 15 doses in an attempt to induce labour in 15 patients. In 10 of these it was successful, delivery occurring within 50 hours. A similar dose was used in 34 patients suffering from uterine inertia and was successful in 30 cases, patients being delivered within 20 hours. [No details are given.] *D. M. Stern*

1634. **Intrauterine Hormone Therapy with Oestrogens. Basic Principles, Experimental Results and Clinical Possibilities.** (Hormonoterapia intrauterina con estrógenos. Fundamentos, resultados experimentales y perspectivas clínicas.)

By A. FERREIRA GÓMEZ. *Rev. esp. Obstet. Ginec.*, **6**, 81–93, 185–199, 273–284, and 339–355, Mar.–Apr., May–June, July–Aug., and Sept.–Oct. 1947. 60 figs. Bibliography.

In view of the frequent failures and disadvantages of oestrogen therapy, the author has made a full experimental and clinical study of the intrauterine use of oestrogens, and reports in detail his findings in a series of articles. Injection of oestrogens into the uterine cornua of both young and castrated adult rabbits resulted in an enormous increase in size of the whole genital apparatus and in particular of the injected cornu. This growth was bigger than that produced by parenteral injection of doses even fifty times greater. The effect was rather more pronounced after oestradiol benzoate than after synthetic oestrogens.

Treatment was carried out in 20 cases—9 of primary amenorrhoea with defective uterine development, 6 of secondary amenorrhoea with a hypoplastic uterus, 3 of uterine atrophy, and 2 of uterine malformation. In 16 cases the treatment was completely successful. The methods of application were the insertion or injection of fluids, pastes, or bougies into the uterine cavity, and the injection of fluids into the uterine wall with a needle. All methods were satisfactory, but the use of bougies was found to be the most convenient. A daily dose of 1 mg. of oestradiol benzoate or stilboestrol repeated up to ten or more times was found to be satisfactory. In 3 cases of secondary amenorrhoea the daily injection of 1 mg. of progesterone into the lumen of the uterus for 3 days after the injection of oestrogen resulted in the occurrence of the secretory phase in the endometrium and in menstruation. The parenteral use of progesterone, as well as of gonadotrophins and vitamin E, and other measures may also be necessary for the establishment of menstruation. In cases of amenorrhoea with a uterus of normal size this route of treatment is not necessary, and other ways of administration are better and more convenient. This method has no disadvantages or dangers, apart from the risk of sepsis present with any intrauterine manipulation and the difficulties of treatment in young patients. The author considers that it should have an important if limited place in treatment in the future, and that the way has been opened up for local treatment with other hormones. *Bryan Williams*

1635. **Changes in Ovarian Function Due to Thiouracil and Methylthiouracil.** (Funktionsänderungen des Ovarium durch Thiouracil und Methylthiouracil.)

By R. KOPF, A. LOESER, and G. MEYER. *Klin. Wschr.*, **26**, 202–206, Apr. 1, 1948. 2 figs., 28 refs.

1636. **Oestrogenic Endocrine Disorders.** (Les endocrinoses oestrogènes.)

By J. A. HUET and A. D. HERSCHBERG. *Ann. Endocrinol., Paris*, **8**, 510–533, 1947. 1 fig., Bibliography.

1637. **Ovarian Infantilism.** (Infantilisme ovarien.)

By P. HARVIER, J-J. GOURNAY, J-L. CAMUS, and L. VISSIAN. *Paris méd.*, **88**, 281–286, June 19, 1948. 5 figs., 6 refs.

1638. **Ovarian Insufficiency and Raynaud's Disease.** (Insuficiencia ovariana e doença de Raynaud.)

By G. MASCARENHAS. *Rev. Ginec. Obstet.*, **1**, 262–270, Apr. 1948. 8 figs., 11 refs.

1639. **Menstrual Disturbances.** (Trastornos menstruales.)

By M. M. FOURNIER. *Ginec. Obstet. Mex.*, **3**, 23–38, Jan.–Feb., 1948. 1 fig.

1640. **Significance of the Constitutional Factor in Menstrual Disturbances and Sterility.** (Die Bedeutung des konstitutionellen Faktors bei Regelstörungen und Unfruchtbarkeit.)

By E. STOCKL. *Zbl. Gynäk.*, **69**, 1087–1095, 1947.

1641. **Differential Diagnosis of Amenorrhea.**

By H. LISSER. *Northw. Med., Seattle*, **47**, 349–350, May 1948.

1642. **Post-war Amenorrhoea.** (Ubersichten die Nachkriegsamenorrhöe.)

By T. HEYNEMANN. *Klin. Wschr.*, **26**, 129–132, Mar. 1, 1948. 14 refs.

1643. **Primary Amenorrhoea of Uterine Origin.** (Amenorrea primaria de causa uterina.)

By A. E. MARTINEZ. *Bol. Soc. chil. Obstet. Ginec.*, **12**, 273–276, Nov. 1947. 5 figs.

1644. **Therapeutic and Diagnostic Use of Neostigmine in Secondary Amenorrhoea.** (Die therapeutische und diagnostische Verwendung des Prostigmin bei sekundärer Amenorrhoe.)

By N. ARESIN. *Zbl. Gynäk.*, **69**, 1067–1072, 1947.

1645. **New Combined Hormone Treatment of Secondary Amenorrhoea.** (Eine neue kombinierte Hormonbehandlung der sekundären Amenorrhoe.)

By H. WINKLER. *Zbl. Gynäk.*, **69**, 1057–1066, 1947. 1 fig., 19 refs.

1646. **Causes of Functional Amenorrhoea.** (Uber die Ursachen der funktionellen Amenorrhoe.)

By F. v. MIKULIEZ-RADECKI. *Zbl. Gynäk.*, **69**, 1046–1052, 1947.

1647. **The Nature of Dysmenorrhea.**

By R. TORPIN, R. A. WOODBURY, and G. P. CHILD. *Amer. J. Obstet. Gynec.*, **54**, 766–775, Nov. 1947. 5 figs., 29 refs.

In this paper some of the theories of the aetiology of dysmenorrhoea are briefly reviewed. The Hamilton optical manometer attached to a bag inside the uterus was used for recordings in patients with dysmenorrhoea. The tracings obtained were of two main types, one "organized" with rhythmic variations and the other "disorganized"; a third or mixture of these two was also sometimes seen. Patients in whom either tracing was obtained suffered from severe pain but it was commoner where the curves were of the "disorganized" type. The pressure associated with pain varied considerably, at times being as low as 30 mm. Hg; the average was 180 mm. Hg and the highest recorded level 340 mm. Hg. The pain was severest when a relatively high pressure persisted between the peaks. It was found that the characteristic pain could be produced experimentally either by increasing the size of the balloon or by injections of "pitressin". "Pitocin", histamine, or acetylcholine causes much less uterine activity, and has little effect on the pain. Balloons were inserted simultaneously at different levels into the uterus. The pressure changes were lower in the fundus than in the cervix; it was also noticed that cervical contractions did not necessarily correspond with the muscular activity of the body of the uterus. The authors conclude their paper with a summary of the other factors which in their view "contribute to dysmenorrhoea".

Braithwaite Rickford

1648. **Distortion of the Spiral Artery in the Ovary Associated with Corpus Hemorrhagicum Cysts.**

By S. M. R. REYNOLDS. *Endocrinology*, **40**, 388–394, June 1947. 7 figs., 2 refs.

In some of the rabbits injected with gonadotrophins (see Abstract 1429) multiple large follicles with one or more large cystic corpora haemorrhagica were produced. These were associated with local extensions of the spiral artery proximal to the cyst. The coiled arrangement of the artery was lost for 6 days but was re-established on a larger scale after 9 days. It is suggested that over-growth of the follicle stretches the spiral artery too much, so that the blood pressure transmitted to the arterioles is increased at this point and the corpus haemorrhagicum results.

[This is a fresh view of the cause of corpora haemorrhagica, which have been more often reported than accounted for.]

Peter C. Williams

1649. **Pertubal Intraperitoneal Menstrual Bleeding and its Clinical Significance.** (Uber pertubare, in die Bauchhöhle abfliessende Menstruationsblutung und ihre klinische Bedeutung.)

By B. OTTOW. *Zbl. Gynäk.*, **69**, 1116–1124, 1947.

1650. **Two Cases of Vicarious Menstruation.** (Zwei Fälle von vikariierender Menstruation.)

By G. JELKMANN. *Zbl. Gynäk.*, **69**, 1103–1108, 1947. 15 refs.

1651. **Hormone Implants in the Menopause and Castration.** (Les implantations hormonales dans le ménopause et la castration.)

By R. BOURG. *Scalpel, Brux.*, **101**, 365–372, Apr. 17, 1948.

1652. **Menopausal Menorrhagia and Metrorrhagia and their treatment by Radium.** (Menometrorragias do climatério e seu tratamento pelo radium.)

By A. F. MARTINS. *An. brasil. Ginec.*, **13**, 275–284, Apr. 1948. 9 refs.

1653. **Hormone Treatment of Menopausal Symptoms.** (Hormonbehandling ved klimakteriske besvær.)

By F. BØE. *Nord. Med.*, **38**, 1111–1112, June 4, 1948.

1654. **Value of Pituitary Irradiation in Withdrawal Symptoms at the Menopause.** (Uber den Wert der Hypophysenbestrahlung bei klimakterischen Ausfallserscheinungen.)

By A. KOTEK. *Zbl. Gynäk.*, **69**, 1073–1077, 1947.

1655. **Fibrosis Uteri.**

By R. SHOEMAKER and J. E. KAHLER. *Arch. Path.*, **44**, 621–637, Dec. 1947. 11 refs.

Working in Los Angeles, U.S.A., the authors conducted a histo-pathological study of 27 uteri from patients aged 31 to 52 inclusive. The prominent symptom was menorrhagia. Though some patients were nulliparous, the majority had borne children. The freshly cut surface was finely textured except in the vascular layer. The consistency was abnormally firm, this change affecting the inner one-third to one-half in all cases and in half the series affecting the outer half but only so far as the outer edge of the vascular layer. The endometrium did not show noteworthy changes. From each uterus a block of tissue comprising the whole thickness of the posterior wall was fixed in Zenker's fluid and acetic acid. Use of the trichrome stain of Mallory or Masson revealed a notable increase in collagen content. No increase of elastic fibres or reticulum was found. Such an increase is significant, and, according to the authors, diagnostic for fibrosis uteri when it amounts to 15 per cent in the submucous layer. Slight hypertrophy of individual muscle fibres coexisted in 3 cases. The study establishes the fact that a defect in the submucous layer of the myometrium—a layer shown to have a poor blood supply in the follicular phase (Faulkner, *Amer. J. Obst. Gynec.*, 1945, **49**, 1)—is a causative factor in menorrhagia. *Magnus Haines*

1656. **Mechanism of Metrorrhagia in Ovarian Tumour.** (Le mécanisme des métrorragies dans les tumeurs de l'ovaire.)

By J. MATHIEU. *Rev. franç. Gynec.*, **43**, 85–92, Mar. 1948. 9 refs.

1657. **Studies of the Human Corpus Luteum. Corpus Luteum-endometrial Relationships in Functional Uterine Bleeding.**

By J. I. BREWER and H. O. JONES. *Amer. J. Obstet. Gynec.*, **55**, 18–45, Jan. 1948. 21 figs., 14 refs.

The authors postulate that functional uterine bleeding may occur even if a corpus luteum is present in the ovary. If the life of the latter is prolonged, areas of irregular regression of the endometrium may be found and give rise to bleeding. Such bleeding is an exaggeration of the normal. In other cases the corpus luteum may be normal and the endometrium correspondingly so, except in small localized regions. In these areas bleeding occurs from local blood sinuses and there is a scanty endometrial loss. This may be due either to a local "bleeding factor" or to a locally abnormal response in the endometrium. Eight cases are analyzed. The material was obtained at operation performed during the bleeding phase. Hysterectomy was carried out, and the whole endometrium was therefore examined; either oöphorectomy or resection of the corpus luteum was performed in the same time. *Kenneth Bowes*

1658. **Treatment of Functional Uterine Haemorrhage** (Tratamento das hemorrhagias funcionais uterinas.)

By A. DE CASTRO CALDAS. *Gaz. méd. portug.*, **1**, 175–186, 1948. 16 refs.

1659. **Pathogenesis of Bleeding from Pathologically Hyperplastic Endometrium.** (Zur Pathogenese der Blutung aus dem pathologisch proliferierten Endometrium.)

By V. VASEK. *Zbl. Gynäk.*, **69**, 1095–1103, 1947.

1660. **Nature and Treatment of Vaginismus.**

By J. NOVAK. *Urol. cutan. Rev.*, **52**, 128–130, Mar. 1948.

1661. **Difficulties in Coitus.** (Schwerigkeiten bei ber Kohabitation.)

By F. v. MIKULICZ-RADECKI. *Geburtsh. u. Frauenheilk.*, **8**, 409–423, May 1948.

1662. **Infertility and the Stability of Marriage.**

By F. POPENOE. *West. J. Surg. Obstet. Gynec.*, **56**, 309–310, May 1948.

1663. **Sterility of Unexplained Aetiology.** (Atiologisch ungeklärte Fälle ehelicher Unfruchtbarkeit.)

By H. STIASNY. *Zbl. Gynäk.*, **69**, 1124–1133, 1947.

1664. **The Scope of Radiology in Diagnosis of the Cause of Sterility.** (Possibilità della radiologia nell' accertamento delle cause di sterilità.)

By A. CAPUA. *Recenti Progr. Med.*, **4**, 389–409, May 1948. 11 figs.

1665. **An Approach to the Investigation and Treatment of the Subfertile Couple.**

By C. S. LANE-ROBERTS. *Med. Press*, **219**, 547–550, June 23, 1948.

1666. **Medical Treatment of Sterility.** (La terapia medica della sterilità coniugale.)

By V. PATRONO. *Recenti Progr. Med.*, **4**, 410–424, May 1948. 12 refs.

1667. **Ovarian Dysfunction and Sterility: Physiotherapy.** (Dysfonctionnement ovarien et sterilité. Traitement physiothérapique.)

By M. BORDIER. *Sem. Hôp. Paris*, **24**, 1082–1086, Apr. 30, 1948. 31 refs.

1668. **Effect of Testis Hyaluronidase and Seminal Fluids on the Fertilizing Capacity of Rabbit Spermatozoa.**

By M. C. CHANG. *Proc. Soc. exp. Biol., N.Y.* **66**, 51–54, Oct. 1947. 22 refs.

Thirty-three doe rabbits were inseminated with a minimal effective number of spermatozoa sus-

pended in saline containing purified testis hyaluronidase, or saline and supernatant fluid of heated normal semen containing hyaluronidase, or in saline and semen of vasectomized buck containing no hyaluronidase. Thirty-two does were inseminated at the same time with the same number of sperms collected from the same rabbit but suspended in saline, serving as parallel controls. It was found that it was the seminal fluid, not hyaluronidase, which really increased the fertilizing capacity of spermatozoa.—[Author's summary.]

1669. **Comparison of Rates of Penetration of Unwashed and Washed Spermatozoa in Cervical Mucus.**

By W. T. POMMERENKE and E. VIERGIVER. *Proc. Soc. exp. Biol., N.Y.*, **66**, 161–163, Oct. 1947. 12 refs.

Samples of mucus were aspirated from the cervical canals of healthy young women. Washing of spermatozoa from healthy donors was achieved by centrifuging for 10 minutes at 1,500 r.p.m. a mixture of one volume of semen and five volumes of Ringer's fluid and resuspending in Ringer's fluid. This procedure resulted in some reduction in the number of motile forms and some cell destruction. The rate of penetrability was measured by the method of Lamar, Shettles, and Delfs (*Amer. J. Physiol.*, 1940, **129**, 234). The cycle was divided into pre-ovulatory, ovulatory, and post-ovulatory phases. Average rates of penetration varied from 0.2 to 0.5 mm. per minute, while the highest rate recorded, found in mucus collected in an ovulatory phase, was 1.7 to 2 mm. per minute. Washing did not impair the ability of spermatozoa to penetrate cervical mucus. In 42 specimens of semen from 4 donors no correlation was apparent between the concentration of spermatozoa and the degree of penetrability of the mucus. *Magnus Haines*

1670. **Interrelationships of Spermatozoa Count, Hyaluronidase Titer and Fertilization.**

By B. SALLMAN and J. M. BIRKELAND. *Amer. J. Physiol.*, **152**, 271–279, Feb. 1948. 14 refs.

1671. **Problems of Artificial Insemination.** (Problemi della fecondiazione artificiale.)

By V. A. DI SANT'AGNESE. *Recenti Progr. Med.*, **4**, 369–388, May 1948. 10 refs.

Abnormalities of the Reproductive Organs

1672. **Uterine Anomaly: Duplication of Uterus, Three Tubes and Three Ovaries. Report of a Case.**

By W. N. ROWLEY. *Ann. Surg.*, **127**, 676–680, Apr. 1948. 1 fig., 2 refs.

1673. **A Rare Congenital Malformation: Uterus Unicornis and Unilateral Renal Agenesia.** (Une anomalie congénitale rare: Utérus unicorne vrai et agénésie rénale unilatérale.)

By C. FRILEUX. *Gynécologie*, **44**, 274–278, Nov.–Dec. 1947. 12 refs.

1674. **Inguinal Ectopia of the Ovary.**

By F. B. PACKARD and E. M. RECTOR. *Northw. Med., Seattle*, **47**, 354–355, May 1948. 5 refs.

Infections of the Reproductive Organs.

1675. **Mechanism of Action of Penicillin.** [In Russian.]

By L. I. BUBLICHENKO. *Akush. Ginek.*, No. 1, 35–37, 1948.

1676. **Tissue Therapy of Inflammation in Gynaecology.** [In Russian.]

By V. N. NEKHAEVA. *Akush. Ginek.*, No. 2, 25–27, 1948.

1677. **Blocking of Head's Zones in the Treatment of Acute Gynecological Inflammations.**

By N. P. VERKHATSKY. *Akush. Ginek.*, No. 5, 55–56, 1947.

In 160 cases of acute pelvic inflammation the cutaneous areas of referred pain were infiltrated intradermally with 1 per cent solutions of procaine, amidopyrine, or phenazone. Procaine (2 to 15 ml.) was successful in abolishing pain in 45 out of 60 cases. Amidopyrine (1 to 2 ml.) was found to act better and for a longer time, and was successful in abolishing pain in 60 out of 70 cases. The effect of phenazone was unsatisfactory and negligible for practical purposes. Distilled water was used as a control in 10 cases and had a partial effect in 3 cases. The disappearance of pain after local injection was a good prognostic sign.

Nicolas Tereshchenko

1678. **Contribution to the Study of Genital Warts.** (Contribution à l'étude des végétations vénériennes.)

By J. RUDLOFF. *Ann. Derm. Syph., Paris.*, **8**, 23–25, Jan. 1948. 54 refs.

A useful summary is given of work on the aetiology of genital warts. The author concludes that common hard warts and genital warts are caused by the same virus, the type of lesion depending on the soil in which it is implanted. [There is a full bibliography.] *James Marshall*

1679. **Reactions of the Vulva to Systemic Diseases.**

By J. PARKS and S. MARTIN. *Amer. J. Obstet. Gynec.*, **55**, 117–132, Jan. 1948. 10 figs., 32 refs.

Common skin lesions such as lichen planus, allergic reactions, herpetiform infections, and psoriasis, when involving the vulva may present a greatly distorted picture because of secondary infection and ulceration. Not only should the vulva be inspected, but a thorough search should be made elsewhere for skin lesions, important areas being the lips, mouth, tongue, hair line, axillae, palms of the hands, back, and breasts. The urethra, Bartholin's glands, vagina, and cervix should be searched for infection. In every instance of vulval ulceration the following investigations should be carried out; complete blood count, chemical

analysis of urine, cultures for gonococci and mycotic organisms, and a hanging-drop examination for *Trichomonas vaginalis*. The need for biopsy, venereal disease tests, and chemical analysis of blood depends on the history and characteristics of lesion.

The author describes the vulval lesions encountered in blood dyscrasias, uraemia, diabetes mellitus, vitamin deficiencies, chronic atrophic dermatitis of the vulva, and allergic dermatitis. He emphasizes that, in the treatment of those vulval lesions for which stilboestrol is indicated, local application is as effective as systemic administration, and that with it the patient experiences none of the effects of the uterine changes associated with oral or intramuscular administration.

Anthony W. Purdie

1680. **Tattooing with Mercury Sulfide for Intractable Anal Pruritus with Brief Reference to Vulval Pruritus and Evaluation of Results.**

By R. TURRELL. *Surgery*, **23**, 63–74, Jan. 1948. 13 figs., 7 refs.

The rationale of tattooing with mercuric sulphide in the treatment of pruritus ani is still uncertain, but it is suggested that the mercuric sulphide deposited in the corium impairs the function of the sensory end-organs. A series of 160 cases was treated by tattooing after orthodox methods had failed; 93 of these are analyzed. Seventy patients, who had severe and chronic anal pruritus associated with cutaneous changes, responded well, 15 results being described as "satisfactory" and the rest as "good". Of 23 patients with anal pruritus but without skin changes, 6 obtained satisfactory relief and 17 were not improved at all. Twelve patients with pruritus ani and pruritus vulvae were treated by tattooing of the perianal skin. The vulval pruritus improved sufficiently to render further tattooing unnecessary. Before tattooing is undertaken a patch test for sensitivity to mercury is carried out. A positive result contraindicates tattooing. Anal skin tags are excised and menopausal women are given oestrin. Tattooing is performed under regional analgesia. If skin changes are absent the area affected is marked out before operation. Tattooing should extend into the anal canal as far as the muco-cutaneous junction and for 1 cm. beyond the area of perianal skin affected. A mercuric sulphide paste is applied to the skin and the area tattooed until the skin shows a permanent and uniform red stain. The ordinary instrument of the tattoo artist may be used, but this is tedious, and the author has designed a reciprocating (2,000 strokes a minute) pneumatic tattooing pistol with which the tattooing can be completed in an average case in about an hour. *R. E. Horton*

1681. **New Treatment of Resistant Idiopathic Pruritus Vulvae.** (Nuevo tratamiento del prurito vulvar esencial rebelde.)

By F. AGUIRRE. *Rev. mex. Cir. Ginec. Cancer*, **15**, 395–399, Oct. 1947. 2 figs., 7 refs.

1682. **Pruritus Ani and Vulvae.**

By M. T. VAN STUDDIFORD and L. D. MCLEAN. *New Orleans med. Surg. J.*, **100**, 445–449, Apr. 1948. 10 refs.

1683. **A Study of the Bacterial Flora of the Normal Vagina.** (Posšvní mikroby u žen bez vytoku.)

By J. MALKOVA and I. MALEK. *Ceskoslov. Gynaec.*, **13**, 59–76, 1948. 3 refs.

The authors examined 132 vaginal smears and cultures from 39 women not suffering from noticeable discharge, with a view to assessing the value of the smear alone in diagnosis and to studying the influence of menstruation on the vaginal flora. It was found that the smear gave a sufficiently accurate picture. Bacteria which were found in the cultures but not in the smears were usually aerobes which could be considered as contaminants—mainly *Bacterium coli*, *Streptococcus faecalis*, and a new species described by the authors in 1943 as *Pseudomonas odorans*. The anerobes found were mainly bacteroids, fusobacteria, leptotrichia, and corynebacteria. The menstrual period caused an increase in contaminants, mainly from the intestine (*Bact. coli*), whereas *Str. faecalis* was a much more constant contaminant; as the organisms appear already during the last few days before the onset of the flow, the increase cannot be explained on purely mechanical grounds.

The investigation shows that organisms may be present in the vagina without causing symptoms and without appearing in smears; these organisms may become dangerous, if transferred to other sites (for example, by tubal insufflation or abortion). They may be cultivable only during the menstrual period, but their presence should be suspected if the smear shows, besides Döderlein's bacillus and epithelial cells, an increased quantity of leucocytes. These organisms increase during menstruation, probably because of more favourable internal conditions; in the same way Döderlein's bacillus shows certain changes during menstruation—decrease in quantity and greater frequency of the less physiological R-phase. *A. Rohan*

1684. **A Study of the Antagonism between *Lactobacillus vaginalis* (Döderlein) and other Lactabacilli, and *Penicillium notatum*.** (Ricerche sull'antagonismo tra il *Lactobacillus vaginalis* (Döderlein) e altri lactobacilli, e il penicillium notatum.)

By D. CAZZOLA and A. TARTARA. *Monit. ostet.-ginec.*, **18**, 41–64, Jan.–June, 1947. 36 refs.

The authors are studying the mycotic flora of the female genital apparatus. Several types of the Penicillium species have been isolated, and the frequent presence of *Penicillium notatum* in the vaginal area led the authors to consider a possible biological function of this organism. In this work the relation between the activity of *P. notatum* and Döderlein's bacillus was investigated.

Vaginal secretion was taken from 8 women at various stages of pregnancy; the technique used is given. Tests were made: (1) of the antibiotic action of *P. notatum* on the lactobacilli; (2) of the antagonism between the lactobacilli and filtrates of *P. notatum*; (3) with penicillin; and (4) of the antibiotic action of the vaginal secretion. Colonies were studied anaerobically in glucose-liver-broth and glucose-liver-agar, and aerobically on glucose-liver-agar, serum-milk-peptone-agar, and milk.

Glucose-liver-agar was particularly useful for isolating Döderlein's bacillus. Both lactobacilli and Döderlein's bacillus grew well in glucose-liver-broth and in milk-serum but the former medium gave a more rapid and greater yield. Antagonism exists between the active principle of *P. notatum* and the lactobacilli. This antagonism is related to vaginal conditions and to the dose of penicillin. Döderlein's bacillus and the other lactobacilli studied, together with *Lactobacillus acidophilus*, are to be included in the group of penicillin-sensitive organisms. The authors have also shown that the vaginal secretion has an antagonistic action toward the lactobacilli studied

Rina Saunders

1685. **Mycotic Vulvovaginitis and the Vaginal Fungi. A Report of 280 Patients.**

By C. P. JONES, B. CARTER, W. L. THOMAS, R. A. ROSS, and R. N. CREADICK. *Amer. J. Obstet. Gynec.*, **54**, 738–747, Nov. 1947. 1 fig., 22 refs.

The authors state that there are three groups of yeast or yeast-like fungi which may be found in the vagina—*Monilia, Cryptococcus*, and *Saccharomyces*. These organisms can only be distinguished by the morphological characteristics of colonies grown on special media. *Monilia*, or *Candida* (the name now recommended), is probably the only organism of this type which gives rise to symptoms. The clinical findings and diagnosis are described, and the methods of collecting and culturing specimens from patients are given. Intradermal skin tests and agglutination reactions are of little value in diagnosis. For treatment, a vaginal jelly with a "bentonite" base containing calcium and sodium propionate has given excellent results.

Braithwaite Rickford

1686. **Gonococcic Vaginitis in Children Treated with a Single Injection of Penicillin in Beeswax and Peanut Oil. Report of Twenty Cases.**

By B. G. CLARKE and H. H. EISENBERG. *Amer. J. Dis. Child.*, **74**, 707–710, Dec. 1947. 18 refs.

This paper describes the effects of a single injection of 200,000 Oxford units of sodium penicillin in oil in the treatment of vaginitis in negro children. Altogether 20 patients were treated, but 2 received only 100,000 units. There were no untoward reactions in any case, and cure appeared to be prompt and complete. *Patrick Mallam*

1687. **Trichomonas Vaginalis and its Pathogenetic Character.** (Rzesistek pochwowy (Trichomonas vaginalis) i jego rola chorobotwórcza.)

By A. ETTINGER. *Przeg. Lek.*, **3**, 774–778, Nov. 1947. Bibliography.

1688. **Trichomonas Vaginitis.** (Colpitis tricomoniásica.)

By R. OSORIO Y CARAJAL. *Ginec. Obstet. Méx.*, **3**, 39–44, Jan.–Feb. 1948. 10 refs.

1689. **Trichomonas Vaginalis: Incidence, Signs, Symptomatology and Special Cases.**

By W. McK. H. MCCULLAGH. *Med. Press*, **219**, 469–471, May 26, 1948.

1690. **Diathermy Coagulation in Chronic Cervicitis.** (Fisioterapia con diatermocoagulazione della esocervicite cronica del collo dell'utero.)

By G. M. REVIGLIO. *Ginecologia, Torino*, **14**, 146–152, Mar. 1948.

1691. **Conservation in Treatment of Severe Adnexal Inflammation.** (De la conservation dans le traitement des annexites graves.)

By J. MOUSSELON. *Rev. franç. Gynéc.*, **43**, 105–114, Mar. 1948.

1692. **Morphological Changes in the Fallopian Tubes and Body of the Uterus in Chronic Inflammation.** [In Russian.]

By M. I. MALEVA. *Akush. Ginek.*, No. 2, 1–7, 1948. 6 figs.

1693. **Absorption and Chemical Decomposition of Iodized Oil in the Inflamed Fallopian Tube.** (Resorption und chemischer Abbau des Jodöls in entzundlich veränderten Eiletern.)

By M. KNEER. *Zbl. Gynäk.*, **69**, 959–972, 1947. 9 figs., 13 refs.

1694. **Detection of Latent Genital Tuberculosis by Culture of Menstrual Discharge.**

By I. HALBRECHT. *Lancet*, **2**, 947–948, Dec. 27, 1947. 6 refs.

Endometrial biopsies have shown that latent genital tuberculosis is commoner than hitherto suspected, occurring in at least 5 per cent of cases of primary sterility. Endometrial biopsy, however, can give a positive result only when tuberculosis has reached that particular portion of the endometrium removed for scrutiny. Furthermore, instrumentation is dangerous in such cases, and in 5 cases of tuberculous endometritis in the author's series severe pelvic peritonitis developed after curettage. In view of these objections the author undertook culture of menstrual blood obtained from the fornix and the os with a vaginal speculum on the first or second day of the menses, and repeated his examination at least thrice in each patient. Petragnani's specific culture medium was used. Of 140 tests in 80 women with primary sterility, including 10 with proved endometrial

tuberculosis and 2 others clinically suspected of genital tuberculosis, culture was positive nine times in 6 women. Nineteen other cultures grew non-pathogenic acid-fast bacilli differing from *Mycobacterium tuberculosis* culturally and morphologically. The author suggests that this is the only safe method of establishing the diagnosis where genital tuberculosis is clinically suspected, and that at least three examinations should be carried out in all cases of primary sterility before intrauterine intervention is undertaken. No genital tuberculosis was found in the husbands of any of the women in whom menstrual blood culture was positive.

[Culture of menstrual blood was positive in only 2 of 10 proved cases of endometrial tuberculosis. Its value as a safeguard before operation is therefore limited and endometrial biopsy remains much more likely to yield a true diagnosis.]

J. A. Chalmers

1695. **New Method for Diagnosis of Genital Tuberculosis.** (Un nuevo método para el diagnóstico de la tuberculosis genital.)

By P. DE LA PENA REGIDOR. *Rev. esp. Obstet. Ginec.*, **7**, 119–120, Mar.–Apr. 1948. 2 refs.

1696. **Female Genital Tuberculosis.** (Tuberculosis genital femenina.)

By M. URRUTIA. *Ginec. Obstet. Mex.*, **3**, 139–148, Mar.–Apr. 1948. 4 figs.

1697. **Endometrial Tuberculosis.** (Tuberculose do endométrio.)

By A. CAMPOS DA PAZ FILHO. *Med. Cirurg. Farm.*, No. 144, 163–175, Apr. 1948. 8 figs., 35 refs.

1698. **Diagnosis of Tubal Tuberculosis without Clinical Signs.** (Le diagnostic de la tuberculose tubaire inapparente.)

By J. VABOIS. *C. R. Soc. franç. Gynéc.*, **18**, 80–84, Mar. 1948.

1699. **Tuberculous Salpingitis. Report of a Typical Case.**

By E. C. VEPROVSKY and G. SCHAEFER. *Surg. Clin. N. Amer.*, **28**, 513–516, Apr. 1948.

1700. **Treatment of Acute Salpingitis and Pelvic Peritonitis with Sulphonamides.** (Die Behandlung der akuten Salpingitis und Beckenperitonitis mit Sulfonamiden.)

By I. FALCKENBERG. *Geburtsh. u. Frauenheilk.*, **8**, 369–372, Apr. 1948. 3 refs.

New Growths of the Reproductive Organs.

1701. **Method of Staining Vaginal Smears.** (Método práctico de coloración de frotis vaginales.)

By R. PINEDA. *Rev. esp. Obstet. Ginec.*, **7**, 103–106, Mar.–Apr. 1948. 4 refs.

1702. **Value of the Vaginal Smear in the Diagnosis of Genital Cancer.** (Valor actual del diagnóstico del cáncer genital por los extendidos vaginales.)

By R. G. HERRERA and J. M. E. MEZZADRA. *Prensa méd. argent.*, **35**, 771–772, Apr. 23, 1948. 16 refs.

1703. **So-called Extragenital Chorionepitheliomata.** (Zur Frage der sogenannten extragenitalen Chorionepitheliome.)

By G. MICHEL. *Frankfurt. Z. Path.*, **59**, 59–68, Aug. 2, 1947. 1 fig., 43 refs.

This paper describes another case in which, like those of Prym and Symeonides, a large retroperitoneal "chorionepithelioma" in a male was accompanied by an atrophied testis containing a scarred area devoid of tumour. There is no doubt that in these cases a small primary teratoma of the testis had undergone retrogression after having metastasized.

R. A. Willis

1704. **Hidradenomas of the Vulva. Report of Four Cases with an Evaluation of Them in the Light of Analogous Breast Lesions.**

By J. A. CUNNINGHAM and J. HARDY. *Sth. Surg.*, **13**, 831–838, Nov. 1947. 5 figs., 3 refs.

This paper describes four examples of papillary cystic hydradenoma or sweat-gland tumour of the vulva. Impressed by the structural resemblance of these growths to intraductal papillary tumours of the breast, the authors suggest that the vulval apocrine and sweat glands are developmentally akin to the mammary glands. [This suggestion is not new, and, like many others with phylogenetic implications made by clinicians and pathologists, is purely speculative.]

R. A. Willis

1705. **Hydradenoma and Hydradenocarcinoma of the Vulva.** (Hidradenoma e hidradenocarcinoma da vulva.)

By D. DUARTE. *Rev. Ginec. Obstet.*, **1**, 256–260, Apr. 1948. 1 fig., 9 refs.

1706. **The Prophylaxis of Recurrent Carcinoma of the Vulva.** [In English.]

By P. MALPAS. *Acta radiol., Stockh.*, **28**, 681–690, Nov. 13, 1947. 9 refs.

Recurrences of vulval carcinoma fall into two groups, early and late, appearing either earlier or later than 2 years after radical treatment. This division, according to the author, is justified by the difference of origin of these types of recurrence. Prophylaxis of early recurrence in the vulva itself is by adequate radical excision. The author advocates for this primary operation removal of the vestibule, lower urethra, lower vagina, and a wide area of perineal skin as far back as the anus; the wound is allowed to heal by granulation and no attempt is made to refashion the urethral orifice. Remote metastases in iliac lymph nodes and other organs appear within a few months of radical treatment; if there is no local recurrence it means that radical treatment was instituted too late. Inguinal metastases can be prevented by thorough and complete bilateral inguinal adenectomy. This is

carried out in two stages, the unaffected side being dealt with first. The commonest site of recurrence is at the inner end of the inguinal scar, and to minimize this the author advocates a planned incision extending from about ¼ in. (1.25 cm.) below the inguinal fold and bifurcated at its inner end, one branch extending across the pubic spine to meet the incision of the opposite side at the upper border of the symphysis pubis, and the other extending down to form part of the vulvectomy wound. The wounds are allowed to heal by second intention. Late recurrences always appear in the vulva itself, and they remain local in character. Often the rate of growth is slower than that of the primary. The author is inclined to the view that the local recurrences are in the nature of fresh growths, and that such lesions should be excised. Figures are included giving the total 5-year survival rate. Eleven patients were alive without recurrence after 5 years, and 8 were alive with recurrence, giving a total of 19 out of 38 patients alive after 5 years. *T. Keith Morgan*

1707. **Carcinoma of the Clitoris.** (Carcinoma da clitóride.)

By MONTEIRO and A. A. QUINET. *Obstet. Ginec. lat.-amer.*, **6**, 75–91, Mar.–Apr. 1948. 5 figs., 20 refs.

1708. **Vaginal Fibromata.** (Les fibromes du vagin.)

By G. KROPFF. *Bull. méd., Paris*, **62**, 209–216, May 1, 1948. 2 figs., 18 refs.

1709. **Primary Epithelioma of the Vagina.** (Epitelioma primitivo de la vagina.)

By A. BERGENFREID. *Bol. Soc. chil. Obstet. Ginec.*, **12**, 295–296, Nov. 1947.

1710. **A Study of Cystic Pneumatosis of the Vagina.** (Contributo allo studio della pneumatosi cistico della vagina.)

By A. BLASI. *Arch. Ostet. Ginec.*, **53**, 120–134, Mar.–Apr. 1948. 6 figs., 30 refs.

1711. **The So-called Botryoid Sarcoma of the Vagina in Childhood.** (Sui cosidetti sarcomi a grappolo della vagina nell'infanzia.)

By A. FASANOTTI. *Arch. Ostet. Ginec.*, **53**, 80–104, Mar.–Apr. 1948. 7 figs., Bibliography.

1712. **Two Cases of Axial Torsion of a Uterus with Fibroids.** (A propos de deux observations de torsion axiale d'un utérus fibromateux.)

By F. POILLEUX, —. LEGENDE, and —. KOSKAS. *Gynéc. et Obstét.*, **47**, 335–338, 1948.

1713. **Roentgen Therapy in Uterine Fibromyoma without Ovarian Sterilization.**

By G. E. PFAHLER. *Amer. J. Roentgenol.*, **58**, 798–804, Dec. 1947. 12 refs.

The author records 4 cases of uterine fibromyomata treated successfully by X-ray therapy with ovarian protection. This treatment was followed by pregnancies and the delivery of normal babies. Up to 20 years later the children showed no abnormality. He does not propose this treatment as an alternative to myomectomy, but suggests its use in cases where there are small interstitial fibromyomata and where hysterectomy is the only alternative. In his view the X-rays act directly upon the tumours and not necessarily or primarily upon the ovaries. He briefly surveys the literature of X-ray therapy for fibromyomata in general, and finds confirmation of his view that uncomplicated tumours can be successfully treated by this means.

The 4 cases recorded are of particular interest in that the original irradiation was given respectively in 1915, 1924, 1938, and 1935; in only 1 case did amenorrhoea follow the treatment, and all but 1 of the patients subsequently had one or more healthy children. Details of the technique and dosage are given, but in general only the median portals were used and the ovarian areas were protected by lead filters. The fibroids disappeared completely, and Macfarlane is quoted on the improbability of carcinoma developing in the uterus after radiotherapy for fibroids. *Hugh R. Arthur*

1714. **Cardiovascular Syndromes in Uterine Fibromyomatosis.** (La sindrome cardiovascolare nella fibromiomatosi uterina.)

By F. CASSANO and C. CONTI. *Monit. ostet.-ginec.*, **19**, 22–82, Jan.–Feb. 1948. 10 figs., Bibliography.

1715. **Structure and Pathogenesis of Polypoid Tumours of the Uterus.** (Considerazioni sulla struttura e sulla patogenesi dei tumori polipoidi dell'utero.)

By S. PRINCIPE. *Monit. ostet.-ginec.*, **19**, 13–21, Jan.–Feb. 1948. 2 figs., 8 refs.

1716. **Comparative Value of Deep and Supervoltage Roentgen Therapy. Statistical Analysis of Five Year Results in Selected Groups.**

By T. LEUCUTIA. *Amer. J. Roentgenol.*, **58**, 347–356, Sept. 1947. 15 refs.

The results of 15 years' experience of supervoltage therapy at Harper Hospital, Detroit, are discussed. Physical investigations show that a greater depth dose is attained than with deep X-ray therapy, so that skin reaction is diminished, irradiation is more homogeneous, and fewer ports of entry are required. A review of the literature reveals improvements in the results of treatment of carcinoma of the cervix, bladder, larynx, and rectum.

The present study is based on a series of 1,888 cases treated from 1923 to 1940, of which 1,038 received deep X-ray therapy and 850 supervoltage X-ray therapy. All cases are included, even where palliation only could be expected. The factors of supervoltage X-ray therapy were 500 kV (constant) 7 mm. Cu, 3 mm. Al, 3 mm. celluloid, half-value-layer 9 mm. Cu, intensity of 20 r per minute at 60 cm. skin-target distance.

A comparison is made of cases treated by both methods. No improvement in results was noted in cases of carcinoma of the tongue or thyroid and

only slight improvement in cases of carcinoma of bladder and larynx. Carcinoma of the cervix is treated by a combination of radium with X-ray therapy to supplement the dose at the periphery of the pelvis. With supervoltage therapy the 5-year survival rate has increased from 20 to 40 per cent. In cases of carcinoma of the fundus uteri treated by surgery combined with pre-operative and post-operative irradiation the 5-year survival rate is 50 per cent with supervoltage as against 40 per cent with deep X-ray therapy. In cases of carcinoma of the ovary postoperative irradiation gives a 5-year survival rate of 17 per cent with deep therapy and 32 per cent with supervoltage therapy. The 5-year survival rate in inoperable cases of carcinoma of the rectum treated solely by X-ray therapy increased from 10 to 20 per cent. The author notes that less skin damage is observed with supervoltage therapy, and suggests that while it involves no new principle it is the irradiation method of choice for the small tumour located in a large volume of tissue.

D. G. Bratherton

1717. **Carcinoma of the Body of the Uterus.**
By R. A. McGILL. *J. Oklahoma med. Ass.*, **41**, 177–180, May 1948. 13 refs.

1718. **Carcinoma of the Body of the Uterus in Association with Fibroids.** (El cáncer del cuerpo en las fibromatosis uterinas.)
By C. C. VERGARA. *Ginec. Obstet. Mexico*, **3**, 115–128, Mar.–Apr. 1948. 14 figs., 12 refs.

1719. **Chorionepithelioma of the Uterine Cervix.** (Chorio-epitheliome du col utérin.)
By R. ROUCHY. *C. R. Soc. franç Gynéc.*, **18**, 76–78, Mar. 1948. 1 fig.

1720. **Cervical Erosion and Carcinoma.** (Erosio colli uterig og carcinom.)
By W. MUNCK. *Nord. Med.*, **38**, 1115–1117, June 4, 1948. 21 refs.

1721. **Simultaneous Cancer of the Cervix and Lesser Curvature of the Stomach.** (Cancer double du col uterin et de la petite courbure de l'estomac.)
By C. MASSIAS and NGUYEN DINH-HAO. *Bull. Ass. franç Cancer*, **35**, 125–126, 1948.

1722. **Early Diagnosis of Cervical Carcinoma.**
By C. E. GALLOWAY. *Mississippi Valley med. J.*, **70**, 93–97, May 1948.

1723. **A Comparison of the Accuracy in Diagnosis of the Vaginal Smear and the Biopsy in Carcinoma of the Cervix.**
By R. M. GRAHAM, S. H. STURGIS, and J. McGRAW. *Amer. J. Obstet. Gynec.*, **55**, 303–307, Feb. 1948. 12 refs.

Out of 181 cases of carcinoma of the cervix diagnosis was established in 148 by a positive vaginal smear (Papanicolaou) and positive cervical biopsy. There were 19 "false negative" biopsies and 17 "false negative" smears. In 3 cases both methods failed. There were three chief reasons for failure of biopsy: (1) tissue taken from the wrong area; (2) an error in interpretation of the specimen submitted; (3) not enough tissue taken for diagnosis. Vaginal smear may fail to establish the diagnosis because some tumours do not desquamate cells into the vagina. In others the cells may be present on the slide but may not be seen; lastly malignant cells may be misinterpreted as benign. By a combination of the two methods the correct diagnosis may be expected in 99 per cent of cases.

D. M. Stern

1724. **Preinvasive Carcinoma of the Cervix Uteri. Seven Cases in which it was Detected by Examination of Routine Endocervical Smears.**
By E. R. PUND, H. E. NIEBURGS, J. B. NETTLES, and J. D. CALDWELL. *Arch. Path.*, **44**, 571–577, Dec. 1947. 4 figs., 8 refs.

Seven cases are described in which pre-invasive carcinoma of the cervix was diagnosed by stained smears of the endocervix obtained by twirling a cotton applicator (throat swab) over the area, including any erosion. Staining was by the method of Papanicolaou (*J. Amer. med. Ass.*, 1946, **131**, 372), which offers the best method of detecting malignant cells in the circumstances. Each diagnosis was checked by biopsy. The authors, working in Georgia, U.S.A., are extending their study to determine whether all cancers of the cervix can be diagnosed in the early stages, and intend to compare results obtained on this basis with the incidence reported by Pund and Auerbach (*J. Amer. med. Ass.*, 1946, **131**, 960) of pre-invasive cancer in 3.9 per cent of 1,200 surgically removed cervices. In smears which suggest the presence of, or are positive for, cancer a biopsy or endocervical curettage must be carried out.

Magnus Haines

1725. **The Microscopic Criteria for the Diagnosis of Early Carcinoma of the Cervix Uteri.**
By E. E. GURSKIS, D. C. BEAVER, and H. M. NELSON. *Surg. Gynec. Obstet.*, **85**, 727–733, Dec. 1947. 8 figs., 5 refs.

Fifteen specimens of early carcinoma of the cervix uteri and the cellular changes in the pre-invasive stage are described. In some specimens the transition from normal to cancerous epithelium was abrupt, in others gradual. [The photomicrographs show undoubted carcinoma; the authors do not discuss the difficulties of distinguishing between early carcinoma and non-cancerous hyperplasias and metaplasias of the cervical epithelium.]

R. A. Willis

1726. **The Use of the Vaginal Smear in the Diagnosis of Cancer.**
By H. ULFELDER. *Connecticut med. J.*, **12**, 513–514, June 1948. 10 refs.

1727. **Prognosis in Carcinoma of the Uterine Cervix.**
By A. N. ARNESON. *J. Tennessee med. Ass.*, **41**, 195–205, June 1948. 9 figs., 8 refs.

1728. **Is the Prognosis of Cervical Carcinoma Definitely Related to its Degree of Spread?** (Ist die Prognose des Kollum-Karzinoms durch seine räumliche Ausbreitung eindeutig bestimmt?)
By H. REICHENMILLER, G. MUNST, and H. HAILE. *Geburtsh. u. Frauenheilk.*, **8**, 198–206, Jan. 1948. 2 figs., 13 refs.

It is usual to give a favourable prognosis in cases of carcinoma of the cervix in stages I and II and a less favourable prognosis in stage III, yet sometimes, even in stage I, the disease progresses rapidly and the prognosis is incorrect. The authors have endeavoured to find a more accurate manner of assessing the prognosis.

They investigated in various ways 631 cases of carcinoma of the cervix treated at the University Clinic, Tubingen. The patients were divided into three groups according to their state of health when they first came under observation: (1) cachectic; (2) apparently healthy; (3) without any specific feature. The majority of women in this group were of the peasant class, had lived a hard life, working long hours, and were thin and prematurely aged. One-sixth of the patients were in group 1, one quarter in group 2, and more than half in group 3. The ultimate prognosis was poor in group 1. Only 25 per cent of those in stage I were alive at the end of 5 years, as against 11.8 per cent in stage II and 4.1 per cent in stage III. The prognosis in group 2 was better. In stage I the cure rate was 66 per cent, in stage II it was 42.6 per cent, and in stage III it was 27.3 per cent. The prognosis in group 3 was only slightly less favourable than in group 2. In stage I the cure rate was 49 per cent; in stage II, 41 per cent, and in stage III, 21 per cent. The authors conclude that the appearance of cachexia is associated with an unfavourable prognosis, no matter what the stage of the disease.

The relation between the age of the patient and the extent of the disease when the patient was first seen was also studied. The disease was nearly always more advanced in the old patient, who tended to seek advice late. The ultimate prognosis was better, however, in these patients than in women under the age of 35. The authors considered also the connexion between the age of the patient and the histological picture. The common tumour contained the undifferentiated one-cell type of flattened epithelial cell. This was present in over half of the cases. In patients between the ages of 41 and 50 the unripe proliferative flattened epithelial carcinoma, the unripe carcinoma with epithelial nests and columns, and the completely undifferentiated carcinoma are the common types, while in women aged 60 or over the ripe flattened carcinoma with cornification, the adenocarcinoma and the unripe carcinoma are the usual types. In other words the more rapidly growing carcinoma occurs in the younger women and the more highly differentiated slow-growing tumour in the older women. Further investigations must be carried out before a more accurate prognosis in carcinoma of the cervix can be given. *Gladys Dodds*

1729. **Carcinoma of the Cervix: A Discussion on the Value and Techniques of Supplementary X-ray Therapy.**
By J. G. WINTERNITZ *et al. Brit. J. Radiol.*, **21**, 27–40, Jan. 1948. 27 figs., 16 refs.

This paper describes the techniques of X-ray therapy now practised at 17 centres in Britain, and discusses their shortcomings in relation to overdosage and underdosage of the zones of irradiation by radium, where standardized techniques are used without regard to individual variations in each case. The present method at the Royal Cancer Hospital, London, is an ingenious development of that of Sandler, which attempted to fix, in relation to the pelvis, the volume-dose distribution for any given radium technique. By this method the authors attempt: (1) To assess the "summated dose" of both radium and X-rays at any given site. (2) To use this knowledge to plan the most suitable treatment for each patient, so as to avoid too high or too low a dose. (3) To enable the results of treatment to be assessed in the light of the tumour-dose received much more correctly than has been possible in the past. (4) To make it possible to judge whether there is any value in supplementary X-ray therapy in cases where carcinoma of the cervix has spread to involve lymph nodes. They employ a number of mechanical devices in their method, which are complicated to describe but which are probably simple to use.

[This paper represents a real advance in a subject in which there has been little progress for many years. The original paper, which is well illustrated, must be consulted for details of technique.]
B. Sandler

1730. **Analysis of Technical Factors and Results of Treatment in Carcinoma of the Cervix Uteri. Description of Improved Radium Applicator.**
By G. E. RICHARDS. *Amer. J. Roentgenol.*, **58**, 783–797, Dec. 1947. 6 figs., 5 refs.

The author sets out to answer four questions and to describe a new radium applicator for use in carcinoma of the cervix. First, he compares the best results of surgery with those of radiotherapy. The figures of Bonney and of Taussig are compared with those of the Manchester Radium Clinic for 1938 and with the Toronto figures for 1929–40, and the conclusion is reached that as regards absolute 5-year cure rate radiotherapy can show slightly better results than surgery and carries a lower primary mortality and morbidity. [This section is fraught with all the usual statistical difficulties of such a comparison and no mention is made of the place of surgery in the radio-resistant type of

tumour.] The second question is whether the technique of radiotherapy is at a standstill: the author compares the radiotherapy cure rate figures of various hospitals 15 years ago with those recently reported, and shows that there seems to have been an improvement of about 20 per cent in the Stage I and II cases and of 5 to 6 per cent in the Stage III cases during that period. The third question is the possibility of further improvement. He suggests that improvement may be achieved by: (1) more careful application of physical principles; (2) more skill in applying radium and combining it with X-rays; and (3) the use of new radioactive substances which are in process of development. Expanding the first point, he quotes Todd and Meredith and also Neary in describing the accurate planning of dosage from preliminary pelvimetry and the location of the points in the pelvis requiring maximum intensity of irradiation within the safety limit. He mentions points A and B, lying 2 and 5 cm. laterally from the cervix, and notes that the maximum dose at point A must not exceed 7,500 r because of the proximity of the ureter. He also notes that the maximum dose at point S, in the recto-vaginal septum, must not exceed 5,000 r. He himself designates the lateral pelvic wall as point C and states that the minimum effective dose at this point is 5,000 r. The author stresses that it is impossible to give a dose of 5,000 r or more to the lateral wall by the use of radium or X-rays alone and suggests a combination of both. He favours X-ray therapy before the use of radium, because the bulk of the tumour is thus reduced and infection controlled before the radium is put in, and further, because an adequate test of the radiosensitivity of the tumour is made; he therefore advocates preliminary X-ray therapy in all cases except those in Stage I and some in Stage II. A full description of the deep X-ray therapy technique is given. The interval between X-ray therapy and radium therapy is discussed; in normal cases 3 to 4 weeks is considered optimal, otherwise the tumour may pass the stage of maximum regression and the cervix and vaginal vault may contract. With complications such as severe skin reaction or proctitis or cystitis the interval must be sufficient to allow these to settle down. The author criticizes present radium applicators as being inflexible, insecure, and dangerous to the operator and describes a new applicator. This consists, in its most recent form, of a nylon "bridge" containing radium at each end, having two holes in the middle of the bridge to receive a fork for holding the applicator in place and having a built-in filter of suitable material to protect the rectum; the claim is made that this reduces the intensity of radiation reaching the rectum by 25 to 30 per cent. The lower end of the fork protrudes from the vulva and is attached to a belt worn by the patient. A tandem intrauterine tube is used in conjunction with this applicator, and a self-retaining catheter is inserted before the belt is finally fixed. The radium dosage is calculated in each case, having regard to the previous X-ray dosage, and is built up to give the maximum lethal or tissue-tolerance dose at the special points previously mentioned. In the average case the intrauterine applicator is loaded with 40 mg. in a 1-mm. platinum filter and the vaginal applicator with 30 m. × 2 in 1.5-mm. platinum filters, thus giving 3,500 mg. hours in 87½ hours; a table shows the dosage in r units at the special points with this amount of radium, and two examples are given of total dosages of X-rays and radium. An isodose pelvic chart of final total doses is reproduced and a clinical chart for records is also shown. There is a final general note on the possible technique and dangers of new and more powerful radioactive substances.

Hugh R. Arthur

1731. **Some Aspects of the Results of Radiation Treatment of Carcinoma of the Cervix Uteri.**

By I. LAMPE. *Amer. J. Roentgenol.*, **58**, 651–662, Nov. 1947. 2 figs.

This article discusses survival in patients with carcinoma of the cervix uteri by means of survival curves for a total number of 1,225 patients treated over 12 years. An attempt is made to classify the cases according to anatomical spread and histopathology, with a view to assessing the influence of these factors on end-results. The author concludes that with increasing anatomical extent of the neoplasm the survival rate decreases, but there is no evidence to show that the grades of histopathological differentiation have any marked influence. He also concludes that prediction of 5-year results by study of 3-year survival figures may be misleading. He introduces a new technique of "standardized curves". These are produced by determining the percentage frequency of distribution, as regards anatomical extent, in the whole series. This frequency is then applied to the cases for each individual year, so eliminating the influence of variation from year to year in the distribution of patients in various stages of the disease. The 5-year survival rate in 1,225 patients has risen from 20–25 to 40 per cent over a period of 12 years.

[This seems to be a successful method of assessing this factor, but account has not been taken of a factor equally important—the variation in size of the vagina and its effect on tumour dose delivered by vaginal radium—though the author mentions that contraction of the vaginal apex may prevent the use of routine applicators. Although attention was called some years ago to this factor (Sandler, *Brit. J. Radiol.*, 1942, **15**, 20, and *Proc. R. Soc. Med.*, 1945, **38**, 175), the author states that "the most important factor determining the probability of eradication of carcinoma of the cervix is the anatomical exent of the neoplasm". The evidence quoted suggests that vaginal size has an equally important effect (see also Lederman and Lamerton,

Brit. J. Radiol., 1948, **21**, 11). It would seem that these tables are not completely standardized unless the factor of varying vaginal size is also eliminated.]

B. Sandler

1732. **Rectal Hemorrhage following Irradiation for Carcinoma of Cervix.**

By J. R. JOHNSTON and H. W. JACOX. *Amer. J. Obstet. Gynec.*, **55**, 891–893, May 1948. 1 ref.

1733. **A Rare Metastasis After Radical Operation for Carcinoma of the Cervix.** (Eine seltene Metastase nach radikal operiertem Karzinom des Collum uteri.)

By F. NEMEC. *Krebsarzt*, **3**, 213–216, June 1948. 2 figs., 2 refs.

1734. **A Typical Endometrial Hyperplasia Simulating Adenocarcinoma.**

By E. NOVAK and F. RUTLEDGE. *Amer. J. Obstet. Gynec.*, **55**, 46–63, Jan. 1948. 16 figs., 9 refs.

This is a paper on a subject which perplexes the practising gynaecologist from time to time—is the change seen in some tissue obtained by curetting atypical hyperplasia or adenocarcinoma? Normally the contrast between a carcinomatous area and the surrounding tissue is obvious, but atypical hyperplasia may make the diagnosis very difficult. Confusion may arise from increased number, crowding, and moderately atypical appearance of glands; stratification and abnormal staining of cells; and the presence of squamous plaques in the walls of the glands. The authors review 44 instances of these lesions and have correlated them with the clinical findings and histories.

[A very interesting article.] *Kenneth Bowes*

1735. **Endometrial Changes Resembling Adenocarcinoma, Coinciding with Oestrin Treatment and Granulosa-cell Tumour of the Ovary.** [In English.]

By J. CLEMMESEN. *Acta obstet. gynec. scand.*, **27**, 384–389, 1948. 4 figs., 3 refs.

1736. **Endometriosis.**

By R. S. CRON. *J. Iowa med. Soc.*, **38**, 231–233, June 1948.

1737. **A Study of Endometriosis.** (Contribución al estudio de la endometrosis.)

By R. C. OVARZUN. *Rev. mex. Cir. Cancer*, **15**, 313–320, Aug. 1947.

1738. **Observations on the Study of Endometriosis in Mexico.** (Contribucion al estudio de la endometriosis en México.)

By M. M. BASAURI. *Gynec. Obstet. Mex.*, **3**, 13–22, Jan.–Feb. 1948. 8 figs., 20 refs.

1739. **Endometriosis of the Bladder.**

By H. L. TOLSON and B. SKITARELIC. *Urol. cutan. Rev.*, **52**, 144–147, Mar. 1948. 2 fig., Bibliography.

1740. **Endometriosis of the Bladder. Report of a Case.**

By H. E. SCHMITZ and G. R. BABA. *Urol. cutan. Rev.*, **52**, 124–128, Mar. 1948. 17 refs.

1741. **Endometriosis of the Ileum.**

By A. B. KATZ. *Amer. J. digest. Dis.*, **15**, 162–164, May 1948. 3 figs., 5 refs.

1742. **Endometriosis as Cause of Small Bowel Obstruction. A Report of Three Cases.**

By E. L. ZANDER, V. D'INGIANNI, and E. L. DREWES. *J. int. Coll. Surg.*, **11**, 149–153, Mar.–Apr. 1948. 2 figs., 6 refs.

1743. **Endometriosis as a Cause of Obstruction of the Intestine.**

By P. MCGUFF. *Proc. Mayo Clin.*, **23**, 215–221, Apr. 28, 1948.

1744. **Aberrant Endometrial Tissue and Intussusception.**

By E. M. SOUTHERN. *Brit. med. J.*, **1**, 1178–1180, June 19, 1948. 4 figs., 16 refs.

1745. **Endometriomata of the Sigmoid Colon Simulating Carcinoma.**

By T. FARRAR. *Memphis med. J.*, **23**, 108–109, June 1948. 4 refs.

1746. **Histological Studies of Chocolate Cysts.** (Mikroskopische Studien an Schokoladenzysten.)

By A. VOGE. *Geburtsh. u. Frauenheilk.*, **7**, 48–56, and 87–94, Oct. and Nov. 1947. 11 figs., 34 refs.

The paper describes, with illustrations, a study of 50 chocolate cysts of the ovaries, in all of which endometrium-like glandular tissue was found. The appearance of this tissue varies. When completely enclosed by ovarian tissue the glands remain in the proliferative state, but when discharging into tarry cysts they show cyclical changes resembling those of the uterine endometrium. Serial sections disclosed tubal endometriosis in several cases. The author sees in his findings strong support for Sampson's hypothesis of the origin of tarry cysts. Disseminated foci in other parts of the pelvis often accompany tarry cysts of the ovaries.

R. A. Willis

1747. **Conservation of Ovarian Tissue in Bilateral Ovarian Cysts.** (La conservation du tissue ovarien dans les kystes de l'ovaire bilatéraux.)

By A. J. BRET. *Rev. franç. Gynéc.*, **43**, 133–136, Apr. 1948.

1748. **The Granulosa Cell Tumour of the Ovary. Report of two Cases.**

By H. K. TOPPOZADA. *J. R. Egypt. med. Ass.*, **31**, 230–241, Mar. 1948. 3 figs., 51 refs.

1749. **Ascites and Hydrothorax with Lower Abdominal Tumours (Meigs's Syndrome).** (Ascites en hydrothorax bij gezwellen onder in de buik. Het sydroom van Meigs.)

By G. BLOMHERT and L. P. KIAN. *Ned. Tijdschr. Geneesk.*, **92**, 1523–1532, May 22, 1948. 48 refs.

1750. **A Case of Dysgerminoma with Description of Recurrence.**

By R. B. DURHAM, D. F. ADCOCK, and C. A. SWEATMAN. *J. South Carolina med. Ass.*, **44**, 190–192, June 1948. 1 fig., 6 refs.

1751. **Carcinoma Ovarii and Cerebellar Degeneration.**

By B. BROUWER and F. G. SCHLESINGER. *Proc. K. Akad Wet., Amsterdam*, **50**, 1329–1334, Dec. 1947. 6 figs., 12 refs.

Cases of subacute diffuse cerebellar degeneration are rare. Apart from the members of a single family, all the patients so far reported have also suffered from carcinoma. In the case here described a patient, aged 51, with ovarian carcinoma, began to show cerebellar symptoms about 15 months before death. Psychical disturbances were also present at the beginning but regressed. As in other reported cases the cerebro-spinal fluid contained an excess of protein and gave colloidal reactions of mild paretic type. Postmortem examination revealed a carcinoma of the left ovary with adnexa, with metastases in the neighbouring part of the abdominal cavity. The cerebellum showed no macroscopical evidence of disease, but microscopically there was complete disappearance of Purkinje cells, with relative preservation of baskets and almost complete integrity of the granular layer. The left dentate nucleus was severely degenerated, as were the ventral part of the right nucleus and to a minor degree the roof nuclei. No degeneration of inferior olives was seen. There was loss of many cells in the vestibular nuclei. Meningeal and perivascular infiltration in relation to the degenerated areas of the cerebellum and brain stem was present in this case as in other reported cases of this type. The authors consider that the metabolic disturbances associated with carcinoma affect parts of the central nervous system which are predisposed to degeneration by abiotrophy in Gowers' sense of the word.

J. G. Greenfield

1752. **Ovarian Metastases in Cancer of the Breast.** (Les métastases ovariennes du cancer du sein.)

By —. DARGENT, —. PAPILLON, and —. GUINET. *Bull. Ass. franç. Cancer*, **35**, 4–19, 1948. 13 figs.

1753. **Symptomless Ovarian Metastases in Cancer of the Breast.** (Métastases inapparentes ovariennes du cancer due sein.)

By P. LAMARQUE and G. ROUX. *Bull. Ass. franç. Cancer*, **35**, 20–25, 1948. 4 figs.

1754. **Arrhenoblastoma.** (Zur Frage der Arrhenoblastome.)

By H. GOGEL. *Krebsarzt*, **3**, 182–190, May 1948. 2 figs.

1755. **Corpus Luteum Cysts with Positive Aschheim-Zondek Test in Urine. Report of a Case.** [In English.]

By N. CLEMETSEN. *Acta obstet. gynec. scand.*, **27**, 402–406, 1948. 8 refs.

1756. **Fibromyoma of the Fallopian Tube.** [In English.]

By T. HØLUND. *Acta obstet. gynec. scand.*, **27**, 390–394, 1948. 1 fig., 15 refs.

1757. **Lipoid Foreign-body Granuloma in the Fallopian Tube after Hysterosalpingography.** (Uber ein Lipoid-fremdkerkörpergranulom im Eileiter nach Hysterosalpingographie.)

By H. OBWEGESER. *Klin. Med., Wien.*, **3**, 363–375, May 15, 1948. 2 figs., 13 refs.

1758. **Adenoma Tubulare Testiculare Ovarii.**

By H. ANKER. *Nord. Med.*, **38**, 1124–1127, June 4, 1948. 2 figs., 8 refs.

1759. **Sarcomatous Degeneration of a Fibroma of the Broad Ligament.** (Dégénérescence sarcomateuse d'un fibrome du ligament large.)

By R. GENDRE. *C. R. Soc. franç. Gynéc.*, **18**, 85–86, Mar. 1948.

Operations.

1760. **Anesthesia with Intravenous Pentothal Sodium and Local Nerve Block in Gynecologic Surgery.**

By J. C. MCCANN. *New Engl. J. Med.*, **237**, 931–936, Dec. 18, 1947. 5 figs., 5 refs.

This is the sixth of a series of papers by this author on the use of local nerve block with procaine to prevent the transmission of stimuli whose effects on respiration and muscular relaxation would otherwise necessitate the use of large amounts of "pentothal sodium" as a sole anaesthetic agent. Stimuli arising in the thoracic segments have the greatest reflex effects on respiration; when these effects are predominantly on the expiratory phase, there is increased tone in the muscles of the abdominal wall. In gynaecological surgery these segments are only stimulated during the actual opening and closing of the abdomen; during the rest of an operation such as hysterectomy the stimuli arise in lumbar and sacral segments, have a less violent effect on respiration and abdominal muscle tone, and can be blocked in their course through the utero-sacral ligament by 1 per cent procaine infiltration. This thesis is elaborated on the basis of 450 gynaecological operations (236 of them intra-abdominal), in the course of which the rate of utilization of pentothal, the character of respiration, abdominal muscle tone, and sites of origin to reflex stimuli were examined in detail. It is concluded that the rate of utilization of pentothal is halved by the use of local nerve blocks in such operations.

John Challis

1761. **Surgical Treatment of Genital Prolapse.** (Příspěvek k operační léčbě genitálního prolapsu.)

By J. SYNEK. *Ceskoslov. Gynaek.*, **12**, 359–367, 1947. 4 figs.

The author describes his method of dealing with prolapse during the child-bearing years. It is essentially the same as Fothergill's (Manchester) operation, except that the sacro-uterine ligaments are also fixed to the sides of the uterus. In 68 cases the author has not observed any recurrence of prolapse, although in 4 of his earlier cases a cystocele recurred. *A. Rohan*

1762. **Abdomino-perineal Construction of Artificial Vagina from Rectum.** (Colporretoplastia abdomino-perineal.)

By C. SALGADO. *An. brasil. Ginec.*, **13**, 173–182, Mar. 1948. 2 figs.

1763. **Construction of an Artificial Vagina from the Rectum by a Modified Schubert Technique.** (Création d'un néo-vagin aux dépens du rectum suivant la technique de Schubert modifiée.)

By G. COTTE and P. SANTY. *Lyon chir.*, **43**, 257–265, May–June 1948. 15 figs.

1764. **Culdoscopy, a Useful Gynecologic Procedure.**

By R. W. TELINDE and F. RUTLIDGE. *Amer. J. Obstet. Gynec.*, **55**, 102–116, Jan. 1948. 14 figs., 6 refs.

From time to time the authors have observed the pelvic organs through a peritoneoscope. To overcome the disadvantages of that method, TeLinde in 1940 attempted to obtain a more direct approach by inserting the peritoneoscope through the posterior fornix, with the patient in the lithotomy position, but the result was not satisfactory. Decker in 1944 placed the patient in the knee-chest position so that air might be sucked into the peritoneal cavity to prevent the intestines from interfering with the view of the pelvic viscera. The authors have made frequent use of this method and report their experience in 56 cases.

The instrument consists of a special trocar with a guard on the sheath about 3 cm. from the tip to prevent introduction of the trocar too far. The culdoscope proper consists of a longer metal tube with ocular and objective lenses and a prism to deflect the light so as to make the abdominal contents visible through the ocular lens. Just distal to the objective lens is a small electric bulb, which is illuminated by a dry-cell battery. After careful bimanual examination the patient is placed in the knee-chest position in which she maintains herself or, if anaesthetized, is held (the authors use 2.5 per cent " pentothal sodium " as an anaesthetic). After vaginal and perineal cleansing the perineum is elevated, the vagina balloons out, air enters, and with a quick stab in the middle of the posterior fornix the vaginal mucosa and peritoneum are punctured easily. The obturator is withdrawn and if the tip of the cannula is in the cul-de-sac there will be an audible inrush of air. The sterile culdoscope is then introduced through the cannula. The uterus, tubes, ovaries, broad ligaments, uterosacral ligaments, infundibulo-pelvic ligaments, rectal wall, sigmoid, small intestine, and often the caecum, appendix, and even the ureters may be seen. When examination is completed the culdoscope is withdrawn but the cannula is left in place as the patient assumes the recumbent lateral position. An assistant then presses on the abdomen until the air is exhausted from the abdominal cavity, after which the cannula is withdrawn. The wound in the cul-de-sac is not sutured.

The method has been used mostly in cases in which the history or findings suggested ectopic pregnancy, or in cases of salpingitis simulating tubal pregnancy. It has a useful place, however, in the study of cases of possible endometriosis, selected cases of severe dysmenorrhoea, cases of sterility in which all investigations prove negative, cases of undiagnosed unilateral lower abdominal pain, and cases of post-menopausal bleeding with normal pelvic findings after curettage. The chief contra-indication is the presence of a fixed pelvic mass. *Anthony W. Purdie*

1765. **Surgery of the Cervix with the Electric Knife.**

By J. E. WALLACE. *J. Oklahoma med. Ass.*, **41**, 186–191, May 1948. 7 refs.

1766. **Conservative Surgery in Uterus Bicornis Unicollis.** (La cirugía conservadora del útero monocervical bicorne.)

By R. G. REDONDO. *Toko-ginec. pract.*, **7**, 121–149, Apr. 1948. 16 figs., 3 refs.

1767. **A New Method of Prevention and Treatment of Shock and Infection, with the Object of Lowering Immediate Mortality in Wertheim's Operation.** [In Russian.]

By V. P. MIKHAILOV and A. P. TEREKHOVA. *Akush. Ginek.*, No. 6, 26–31, 1947.

This article embodies the results of 900 Wertheim hysterectomies for carcinoma of the cervix performed in the last 23 years. Details of the stage in which the operation was performed are given for 800 cases—113 patients were in Stage I, 252 in Stage II, 285 in Stage III, and 150 in Stage IV. A more detailed analysis of 751 of these cases is then presented. The over-all primary postoperative mortality was 15.6 per cent (shock 3 per cent, peritonitis 6 per cent, other causes 6.6 per cent). The cases are subdivided into three series: (1) 443 operations (1924–42) with 71 primary deaths, 122 recurrences, and 67 patients alive and well 5 to 18 years after operation; (2) 228 operations (1939–42) with 36 primary deaths, 59 recurrences, and 46 patients alive and well 5 to 7½ years after operation; (3) 80 operations with no primary mortality and, so far, no recurrences. Except for the first 200 cases, all the operations were performed under local analgesia, and in most cases penicillin (100,000 units per litre) was added to the procaine solution as a prophylactic measure against sepsis. No cases of pneumonia occurred among the cases operated on under local analgesia. Shock was invariably present at that stage of the operation when the

uterus and lymph nodes are being dissected out of the pararectal pelvic tissue just before the final removal, and the authors consider that the best method of combating it is to inject intravenously at that moment 2 ml. of a 1 per cent solution of morphine hydrochloride and to give a blood transfusion throughout the operation whether signs of shock are manifest or not.

Nicolas Tereshchenko

1768. **Experiences and Technic in Vaginal Hysterectomy.**

By A. F. LEE. *Northw. Med., Seattle,* **47**, 350–354, May 1948. 7 figs., 5 refs.

1769. **Flap Method of Supravaginal Hysterectomy.** [In Russian.]

By S. B. GOLUBCHIN. *Akush. Ginek.*, No. 2, 20–24, 1948. 2 figs.

1770. **Current Reappraisal of Total Abdominal Hysterectomy.**

By W. J. REICH and M. J. NECHTOW. *Amer. J. Surg.*, **75**, 670–676, May 1948. 12 figs.

1771. **Aneurysm of the Uterine Artery After Subtotal Hysterectomy.** (Anévrysme artériel de l'artère utérine après hystérectomie sub-totale.)

By J. A. PHELIP. *Mém. Acad. Chir., Paris,* **74**, 365–366, May 5–12, 1948

1772. **Tubal Ligations. A Study of 351 Cases.**

By R. J. STOKES. *Bol. Asoc. méd. P. Rico.*, **40**, 104–108, Mar. 1948. 20 refs.

1773. **Influence of Some Gynaecological Operations on Ureteric Function.** [In Russian.]

By Y. V. GUBINSKI. *Akush Ginek.*, No. 2, 15–19, 1948. 2 figs.

1774. **Transvaginal Ureterorectal Anastomosis with Partial Cystectomy: Case Report.**

By H. D. WOLF. *J. Urol.*, **59**, 182–192, Feb. 1948. 10 figs., 2 refs.

The effective treatment of malignant disease of the body of the bladder is a matter of time, but in the case of the trigone of the bladder it is a matter of technique. In the former situation an early growth is disposed of by a partial cystectomy; in the latter situation the involvement of the ureteric orifices or of the internal meatus necessitates some form of urinary diversion. This means that in any case where removal of the growth by cystectomy is undertaken the ureters must be transplanted. In 1935 Hunner first performed transvaginal hysterectomy, cystectomy, and uretero-rectal anastomosis. He reported the case in 1937; it is the only one recorded in the literature. The present author now reports a similar case of transvaginal ureterorectal anastomosis with partial cystectomy for an infiltrating carcinoma of the trigone involving the vesicle orifice. The growth approached to within 1 cm. of the right ureteric orifice and to within 1.5 cm. of the left ureteric orifice. The operation was performed *per vaginam* after a midline episiotomy. Cystectomy was complete except for a small portion of the posterior wall of the body of the bladder. After the ureters had been freed, they were transplanted into the rectum under direct vision through a proctoscope. The wound in the anterior vaginal wall was completely closed, the remaining plaque of the bladder being grafted in. For the ureteric transplantation the usual technique and after-care as for a uretero-sigmoidostomy were followed. The technique of the operation is shown in a series of drawings. At present the patient considers herself well. She has, however, developed herniation of the anterior vaginal wall. *James Kemble*

1775. **The Studdiford Operation for Stress Incontinence in Women.** (A operação de Studdiford na incontinência urinária feminina de esforco.)

By J. A. DE BRITO and O. VAZ. *Med. Cirurg. Farm.*, No. 144, 144–162, Apr. 1948. 9 figs., 19 refs.

1776. **The Treatment of Vesicovaginal Fistula.**

By J. D. GUESS. *Urol. cutan. Rev.*, **52**, 157–159, Mar. 1948. 5 refs.

1777. **Uretero-vaginal Fistula.** [In English.]

By I. MERENYI. *Acta. urol., Budapest,* **2**, 58–61, 1948. 7 refs.

1778. **Rectovaginal Fistula.**

By W. W. PYLE. *J. Tennessee med. Ass.*, **41**, 135–136, Apr. 1948. 4 refs.

1779. **A Condemnation of Resectoscopic Procedures upon the Female Vesical Neck.**

By H. S. EVERETT. *Urol. cutan. Rev.*, **52**, 121–124, Mar. 1948. 6 refs.

Urology

1780. **The Role of the Cystoscope in Gynecology.**

By I. W. KAHN. *Urol. cutan. Rev.*, **52**, 152–156, Mar. 1948.

1781. **The Urinary Disturbances in the Woman, Dependent upon her Genital Apparatus.**

By L. F. RODRIGUEZ MOLINA. *Urol. cutan. Rev.*, **52**, 131–136, Mar. 1948. 13 figs.

1782. **On a Case of Accessory Ureter with an Extravesical Ectopic Orifice, and the Clinical Problems Arising from this Abnormality.** (Uber einen extravesikal mundenden akzessorischen Ureter und die klinischen Probleme dieser Missbildung.)

By G. LANGE. *Z. Urol.*, **40**, 207–246, 1947. 10 refs.

The author describes a case of " ureteric incontinence " (Posner) due to the presence of an accessory ureter with an ectopic opening in the vagina. The patient, a girl aged 5, suffered from involuntary evacuation of urine, despite the apparent presence of sphincteric control, and intermittent voiding of bladder contents. Examination showed the loss

to come from the vagina, but cystoscopy demonstrated the presence of normally functioning right and left ureteric orifices in the bladder. These findings, together with a pyelographic abnormality in the lower part of the course of the left ureter, suggested the diagnosis of an accessory ureter on the left side opening into the internal genital organs. This was confirmed at laparotomy (at the age of 9). The accessory ureter, which drained a separate pelvis at the upper end of the left kidney, was seen to communicate, through a dilated caudal extremity, with a small opening in the left anterior vaginal wall. The ectopic ureter was transplanted into the bladder. Although subsequent progress was satisfactory and incontinence ceased, the implanted ureter was apparently non-functional 2 years later.

A comprehensive review is given of the varieties of accessory and ectopic ureter, including one reference to caudal duplication. The Meyer-Weigert law affecting the position of ectopic ureteric orifices is recapitulated, and lengthy consideration given to the embryological aspects of duplication. Ahlfeld's theory of abnormal fission of the ureteric bud, and Felix's theory based on the observation of several ureteric buds arising from one Wolffian duct (a normal occurrence in some lower vertebrates) are discussed. It is apparent from Chwalla's observations that caudal duplication cannot arise from fission, and must be ascribed to the cranial confluence of two ureteric buds. The remainder of the paper is given up to a statistical review of ureteric abnormalities, and a consideration of their clinical manifestations. Treatment of cases similar to the one recorded is considered under the headings of: (*a*) hemi-nephrectomy and ureterectomy; (*b*) total unilateral nephro-ureterectomy; and (*c*) implantation of the ectopic ureter into the bladder (preferably extraperitoneally). The latter is recommended, but functional results may be disappointing. *J. D. Fergusson*

1783. **Bleeding of Vesical Origin in the Menopause Confused with Uterine and Rectal Bleeding.**
By I. C. RUBIN. *Urol. cutan. Rev.*, **52**, 130–131, Mar. 1948.

1784. **Vesical Neck Obstruction in the Female.**
By J. S. RITTER and L. A. SHIFRIN. *Urol. cutan. Rev.*, **52**, 147–149, Mar. 1948. 9 refs.

1785. **Primary Malignant Melanoma of Female Urethra.**
By J. SAVRAN, E. A. SAYER, and C. E. SCHRADIACK. *Amer. J. Surg.*, **75**, 743–745, May 1948. 2 figs., 7 refs.